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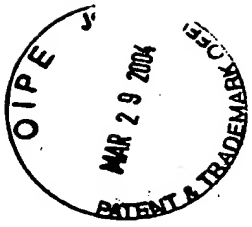
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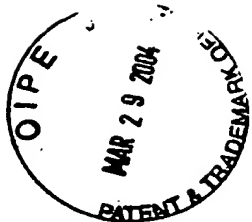
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M K N I K K N Q V M N L G P N S
AAA TTA TTA AAA GAA TAT AAA TCA CAA TTA ATT GAA TTA AAT ATT GAA CAA TTT GAA GCA
K L L K E Y K S Q L I E L N I E Q F E A
GGT ATT GGT TTA ATT TTA GGA GAT GCT TAT ATT CGT AGT CGT GAT GAA GGT AAA ACT TAT
G I G L I L G D A Y I R S R D E G K T Y
TGT ATG CAA TTT CAC TCC AAA AAT AAG GCA TAC ATG GAT CAT GTA TGT TTA TTA TAT GAT
C M Q F E W K N K A Y M D H V C L L Y D
CAA TGG GTA TTA TCA CCT CCT CAT AAA AAA GAA AGA GTT AAT CAT TTA GGT AAT TTA GTA
Q W V L S P P H K K E R V N H L G N L V
ATT ACC TGG GGA GCT CAA ACT TTT AAA CAT CAA GCT TTT AAT AAA TTA GCT AAC TTA TTT
I T W G A Q T F K H Q A F N K L A N L F
ATT GTA AAT AAT AAA CTT ATT CCT AAT AAT TTA GTT GAA AAT TAT TTA ACA CCT ATG
I Y N N K K L I P N N L V E N Y L T P M
AGT CTG GCA TAT TGG TTT ATG GAT GAT GGA GGT AAA TGG GAT TAT AAT AAA AAT TCT CTT
S L A Y W F M D D G G K W D Y N K N S L
AAT AAA AGT ATT GTA TTA AAT ACA CAA AGT TTT ACT TTT GAA GAA GTA GAA TAT TTA CTT
N K S I V L N T Q S F T F E E V C Y L V
AAA GGT TTA AGA AAT AAA TTT CAA TTA AAT TGT TAT GGT AAA ATT AAT AAA AAT AAA CCA
K G L R N K F Q L N C Y V K I N K N K P
ATT ATT TAT ATT GAT TCT AGT AGT TAT CTG ATT TTT TAT AAT TTA ATT AAA CCT TAT TTA
I I Y I I D S M S Y L I F Y N I T K P Y L
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I P Q M M Y K L P N T I S S E T F L K

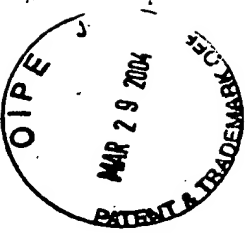
FIG. 1



Bam HI
CCGGATCCATG CAT ATG AAA AAC ATC AAA AAC CAG GTA ATG AAC CTG GGT CCG AAC TCT
H M K N I K K N Q V M N L G P N S
AAA CTG CTG AAA GAA TAC AAA TCC CAG CTG ATC GAA CTG AAC ATC GAA CAG TTC GAA GCA
K L L K E Y K S Q L I E L N I E Q F E A
1. GGT ACT GGT CTG ATC CTG GGT GAT GCT TAC ATC CGT TCT CGT GAT GAA GGT AAA ACC TAC
G I G L I L G D A Y I R S R D E G K T Y
TGT ATG CAG TTC GAG TGG AAA AAC AAA GCA TAC ATG GAC CAC GTA TGT CTG CTG TAC GAT
C M Q F E W K N K A Y M D H V C L L Y D
CAG TGG GTA CTG TCC CCG CAC AAA GAA GGT AAC CAC CTG GGT AAC CTG GTA
Q W V L S P P H K K E R V N H L G N L V
ATC ACC TGG GGC GCC CAG ACT TTC AAA CAC CAA GCT TTC AAC AAA CTG GCT AAC CTG TTC
I T W G A Q T F K H Q A F N K L A N L F
ATC GTT AAC AAC AAA ACC ATC CCG AAC AAC CTG GTT GAA AAC TAC CTG ACC CCG ATG
I V N N K K T I P N N L Y E N Y L T P M
2. TCT CTG GCA TAC TGG TTC ATG GAT GAT GGT GGT AAA TGG GAT TAC AAC AAA AAC TCT ACC
S L A Y W F M D D G K W D Y N K N S T
AAC AAA TCG ATC GTA CTG AAC ACC CAG TCT TTC ACT TTC GAA GAA GTA AAC TAC CTG GTT
N K S I V L N T Q S F T F E V E Y L V
AAG GGT CTG CGT AAC AAA TTC CAA CTG AAC TGT TAC CTA AAA ATC AAC AAA AAC AAA CCG
K G L R N K F Q L N C Y Y K I N K N K P
ATC ATC TAC ATC GAT TCT ATG TCT TAC CTG ATC TTC TAC AAC CTG ATC AAA CCG TAC CTG
I I Y I D S M S Y L I F Y N L I K P Y L
ATC CCG CAG ATG ATG TAC AAA CTG CCG AAC ACT ATC TCC TCC GAA ACT TTC CTG AAA TAA
I P Q M M Y K L P N T I S S E T F L K
TAAGTCGACTGCAGGATCCGGTAAGTAAGTAA
Sall PstI BamHI

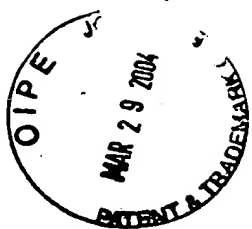
1 and 2: THESE AMINO ACIDS ARE ABSOLUTELY NECESSARY TO PRODUCE CATALYTIC
ACTIVITY. OTHER SUBSTITUTIONS ARE POSSIBLE, SUCH AS DELETIONS
OF THE 10 FIRST AMINO ACIDS. FIG. 2





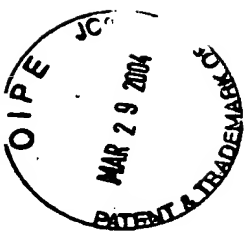
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1747 TTATAGTCCTGTCGGGTTTCGCCACCTCTGACTTGAGCGTCGATTTTGTG ATG CTC GTC AGG GGG GCG GAG 1818
1819 CCT ATG GAA AAA CGC CAG CAA CGC GGC CTT TTT ACG GTT CCT GGC CTT TTG CTG GCC TTT 1878
1879 TGC TCA CAT GTT TCC TGC GTT ATC CCC TGA TTCGTGGATAACCGTATTACCGCCTTTGAGTGAGC 1947
1948 TGATACCGCTCGCCGACGCGAACGACCGAGCGCAGTCAGTGAGCGGAGGAGCGGCCCAATACGCAAC 2027
2028 CGCCTCTCCCCGCGGTTGGCCGATTCATTA ATG CAG CTG GCA CGA CAG GTT TCC CGA CTG GAA AGC 2094
2095 GGG CAG TGA GCGCAACGCAATTA ATG TGA GTTAGCTCACTCATTAGGCACCCCGCTTTACACTTT ATG 2164
2165 CTT CCG GCT CGT ATG TTG TGT GGA ATT GTG AGC GGA TAA CAATTTACACACAGGAAACAGCT ATG 2228
2229 ACC ATG ATT ACG AAT TCT CAT GTT TGA CAGCTTATCATCGATAAGCTTTA ATG CCG TAG TTTATCAC 2295
2296 AGTTAAATTGCTAACGCAGTCAGGCACCGTGT ATG AAA TCT AAC AAT GCG CTC ATC GTC ATC CTC GGC 2363
2364 ACC GTC ACC CTG GAT GCT GTA GGC ATA GGC TTG GTT ATG CCG GTA CTG CCG GGC CTC TTG 2423
2424 CGG GAT ATC CGC CTG ATG GAA CGT GAC GGA CGT AAC CAC CGC GAC ATG TGT GTG CTG 2483
2484 TTC CGC TGG GCA TGC CAG GAC AAC TTC TGG TCC GGT AAC GTG CTG AGC CCG GCC AAG CTT 2543

FIG. 4A



2544 73	ACT	CCC	CAT	CCC	CCT	GTT	GAC	AAT	TAA	TCATCGGCTCGTATA	ATG	TGT	GGA	ATT	GTG	AGC	GGA	2606 7			
	T	P	H	P	P	V	D	N				C	G	I	V	S	G				
2607 8	TAA	CAATTTCACACAGGAAACAGGATCC	BamHI																		
2671 13	AAC	CTG	GGT	CCG	AAC	TCT	AAA	CTG	CTG	AAA	GAA	TAC	AAA	TCC	CAG	CTG	ATC	GAA	CTG	AAC	2730 32
	N	L	G	P	P	N	S	K	L	K	E	Y	K	S	Q	L	I	E	L	N	
2731 33	ATC	GAA	CAG	TTC	GAA	GCA	GGT	ATC	GGT	CTG	ATC	CTG	GGT	GAT	GCT	TAC	ATC	CGT	TCT	CGT	2790 52
	I	E	Q	F	E	A	G	I	G	L	I	L	G	D	A	Y	I	R	S	R	
2791 53	GAT	GAA	GGT	AAA	ACC	TAC	TGT	ATG	CAG	TTC	GAG	TGG	AAA	AAC	AAA	GCA	TAC	ATG	GAC	CAC	2850 72
	D	E	G	K	T	Y	C	M	Q	F	E	W	K	N	K	A	Y	M	D	H	
2851 73	GTA	TGT	CTG	CTG	TAC	GAT	CAG	TGG	GTA	CTG	TCC	CCG	CCG	CAC	AAA	AAA	GAA	CGT	GTT	AAC	2910 92
	V	C	L	L	Y	D	Q	W	V	L	S	P	P	H	K	K	E	R	V	N	
2911 93	CAC	CTG	GGT	AAC	CTG	GTA	ATC	ACC	TGG	GGC	GCC	CAG	ACT	TTC	AAA	CAC	CAA	GCT	ITC	AAC	2970 112
	H	L	G	N	L	V	I	T	W	G	A	Q	I	F	K	H	Q	A	F	N	
2971 113	AAA	CTG	GCT	AAC	CTG	ITC	ATC	GTT	AAC	AAC	AAA	ACC	ATC	CCG	AAC	AAC	AAC	CTG	GTT	GAA	3030 132
	K	L	A	N	L	F	I	V	N	N	K	K	I	I	P	N	N	L	V	E	
3031 133	AAC	TAC	CTG	ACC	CCG	ATG	TCT	CTG	GCA	TAC	TGG	TTC	ATG	GAT	GAT	GGT	GGT	AAA	TGG	GAT	3090 152
	N	Y	L	T	P	M	S	L	A	Y	W	F	M	D	G	G	K	W	D		
3091 153	TAC	AAC	AAA	AAC	TCT	ACC	AAC	AAA	TCG	ATC	GTA	CTG	AAC	ACC	CAG	TCT	TTC	ACT	TTC	GAA	3150 172
	Y	N	K	N	S	T	N	K	S	I	V	L	N	T	Q	S	F	I	F	E	
3151 173	GAA	GTA	GAA	TAC	CTG	GTT	AAG	GGT	CTG	CGT	AAC	AAA	TTC	CAA	CTG	AAC	TGT	TAC	GTA	AAA	3210 192
	E	V	E	Y	L	V	K	G	L	R	N	K	F	Q	L	N	C	Y	V	K	
3211 193	ATC	AAC	AAA	AAC	AAA	CCG	ATC	ATC	TAC	ATC	GAT	TCT	ATG	TCT	TAC	CTG	ATC	TTC	TAC	AAC	3270 212
	I	N	K	N	K	P	I	I	Y	I	D	S	M	S	Y	L	I	F	Y	N	
3271 213	CTG	ATC	AAA	CCG	TAC	CTG	ATC	CCG	CAG	ATG	ATG	TAC	AAA	CTG	CCG	AAC	ACT	ATC	TCC	TCC	3330 232
	L	I	K	P	Y	L	I	P	Q	M	M	Y	K	L	P	N	I	I	S	S	
3331 233	GAA	ACT	TTC	CTG	AAA	TAA	Salt PstI														3404 238
	E	T	F	L	K		TAAGTCGACCTGCAGCCCAAGCTTGGCACTGGCCGCTGCTTTTACACGTCGTGACT														

FIG. 4B



		-2	-1	1				5				10							
		M	H	M	K	N	I	K	K	N	Q	V	M	N	L	G	P	N	S
			20										30						
K	L	L	K	E	Y	K	S	Q	L	I	E	L	N	I	E	Q	F	E	A
			40										50						
G	I	G	L	I	L	G	D	A	Y	I	R	S	R	D	E	G	K	T	Y
			60										70						
C	M	Q	F	E	W	K	N	K	A	Y	M	D	H	V	C	L	L	Y	C
			80										90						
Q	W	Y	L	S	P	P	H	K	K	E	R	Y	N	H	L	G	N	L	Y
			100										110						
I	T	W	G	A	Q	T	F	K	H	Q	A	F	N	K	L	A	N	L	F
			120										130						
I	V	N	N	K	K	I	I	P	N	N	L	V	E	N	Y	L	T	P	M
			140										150						
G	L	A	Y	W	P	M	D	D	G	G	K	W	D	Y	N	K	N	S	I
			160										170						
N	K	S	I	V	L	N	T	Q	S	F	T	F	E	E	V	E	Y	L	V
			180										190						
K	G	L	R	N	K	F	Q	L	N	C	Y	V	K	I	N	K	N	K	P
			200										210						
I	I	Y	I	D	S	M	S	Y	L	I	F	Y	N	L	I	K	P	Y	L
			220										230						
I	P	Q	M	M	Y	K	L	P	N	T	I	S	S	E	T	F	L	K	*

Positions that can be changed without affecting enzyme activity (demonstrated)
positions -1 and -2 are not natural. The two amino acids are added due to cloning strategies

positions 1 to 10: can be deleted
position 36: G is tolerated
position 40: M or V are tolerated
position 41: S or N are tolerated
position 43: A is tolerated
position 46: V or N are tolerated
position 91: A is tolerated
positions 123 and 156: L are tolerated
position 223: A and S are tolerated

Changes that affect enzyme activity (demonstrated)

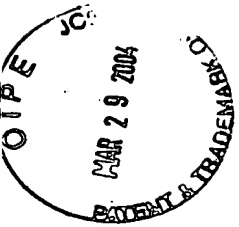
position 19: L to S
position 38: I to S or N
position 39: G to D or R
position 40: L to Q
position 42: L to R
position 44: D to E, G or H
position 45: A to E or D
position 46: Y to D
position 47: I to R or N
position 80: L to S
position 144: D to E
position 145: D to E
position 146: G to E
position 147: G to E

FIG. 5

Group I Intron Encoded Endonucleases and Related Endonucleases

ENDONUCLEASE		RECOGNITION SEQUENCE	CLEAVAGE SITE	▽ INTRON SITE
TWO DODECAPEPTIDE FAMILY (OR 4 BP CUTTERS)	I-Sce I (<i>Saccharomyces</i> mitochondria)	CGC TAGGGATAA CAGGGTAAT ATAGC GCG ATCCCTATTGT CCCATTATATCG		
	I-Sce IV (<i>Saccharomyces</i> mitochondria)	TTCTCATGATTAAGCTCTAATCCATGG AAGAGTAACTAATCGAGATTAGGTACC		
	I-Sce II (<i>Saccharomyces</i> mitochondria)	CTTTGGTCAATCAGAAAGTATATATTT GAAACCACTAGGTCTTCATATATAAA		
	I-Ceu I (<i>Chlamydomonas</i> chloroplast)	TAA CGGTCCIAAGGTAGCGAAATTCA ATTGCCAGGATTCCATCGCTTTAAGT		
	I-Ppo I (<i>Physarum</i> nucleus)	TGACTCTCTTAAAGGTAGCCAAATGCC ACTGAGAGAATTCCATCGGTTTACGG		
	I-Sce III (<i>Saccharomyces</i> mitochondria)	GGAGGTTTTGGTAACTATTTATTACC CCTCCAAAACCATTGATAAATAATGG		
	I-Cre I (<i>Chlamydomonas</i> chloroplast)	GGGTTCAAACGTCGTGAGACAGTTT CCCAAGTTTTGCGAGCACTCTGTCAA		
	Endo. Sce I(RF3) (<i>Saccharomyces</i> mitochondria) (Non intronic)	GATGCTGTAGGCATAGGCTTGTTAT CTACGACATCCGTATCCGAACCAATA		
	HO (<i>Saccharomyces</i> nucleus) (Non intronic)	CTTTCCGCAACAGTATAATTTTATAA GAAAGGCGTTGTCAATTAAAAATATT		
	I-Csm I (<i>Chlamydomonas</i> mitochondria) (Putative endonuclease)	ACCATGGGGTCAAATGTCTTTCTGGG TGGTACCCAGTTTACAGAAAGACCC		
OTHER STRUCTURAL FAMILIES	(Bacteriophage T4)			
	I Tev I	CAACGCTCAGTAGATGTTTTCTTGGGTCTACCGTTTAAAT GTTGCGAGTCATCTACAAAGAACCCAGATGGCAAATTA		
	I Tev II	CAAGCTTATGAGTATGAAGTGAACACGTTATT GTTCGAATACTCATACTTCACTTGTGCAATAA		
	I Tev III	GCTATTCTGTTTTTATGATCTTTTGGCTGTAGCTTTAA CGATAAGCAAAAATACATAGAAAACGCACATCGAAATT		

FIG. 6



EXPRESSION VECTORS

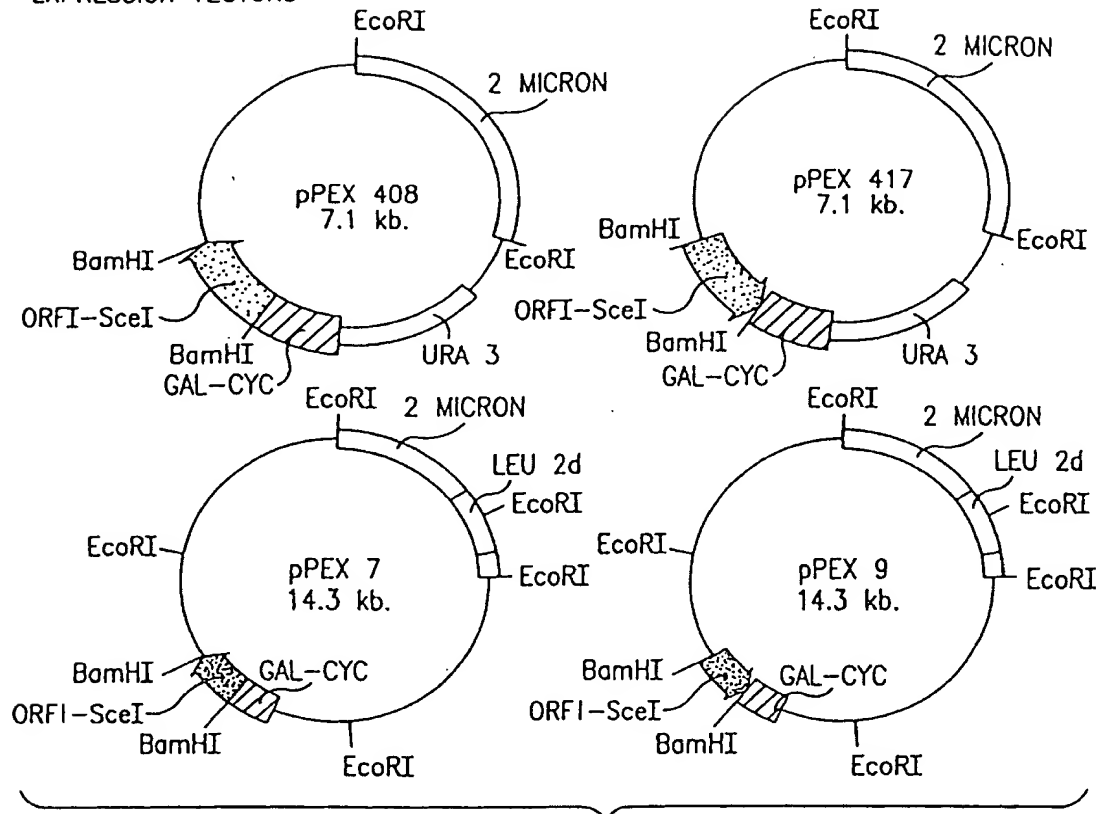


FIG. 7

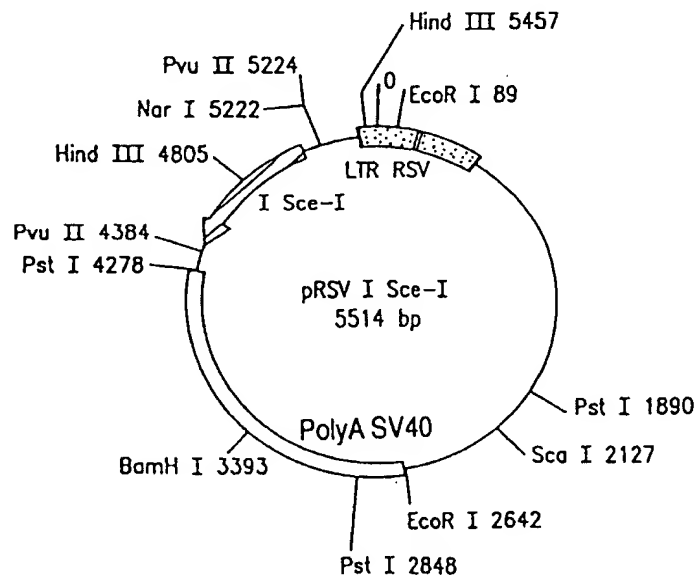


FIG. 8

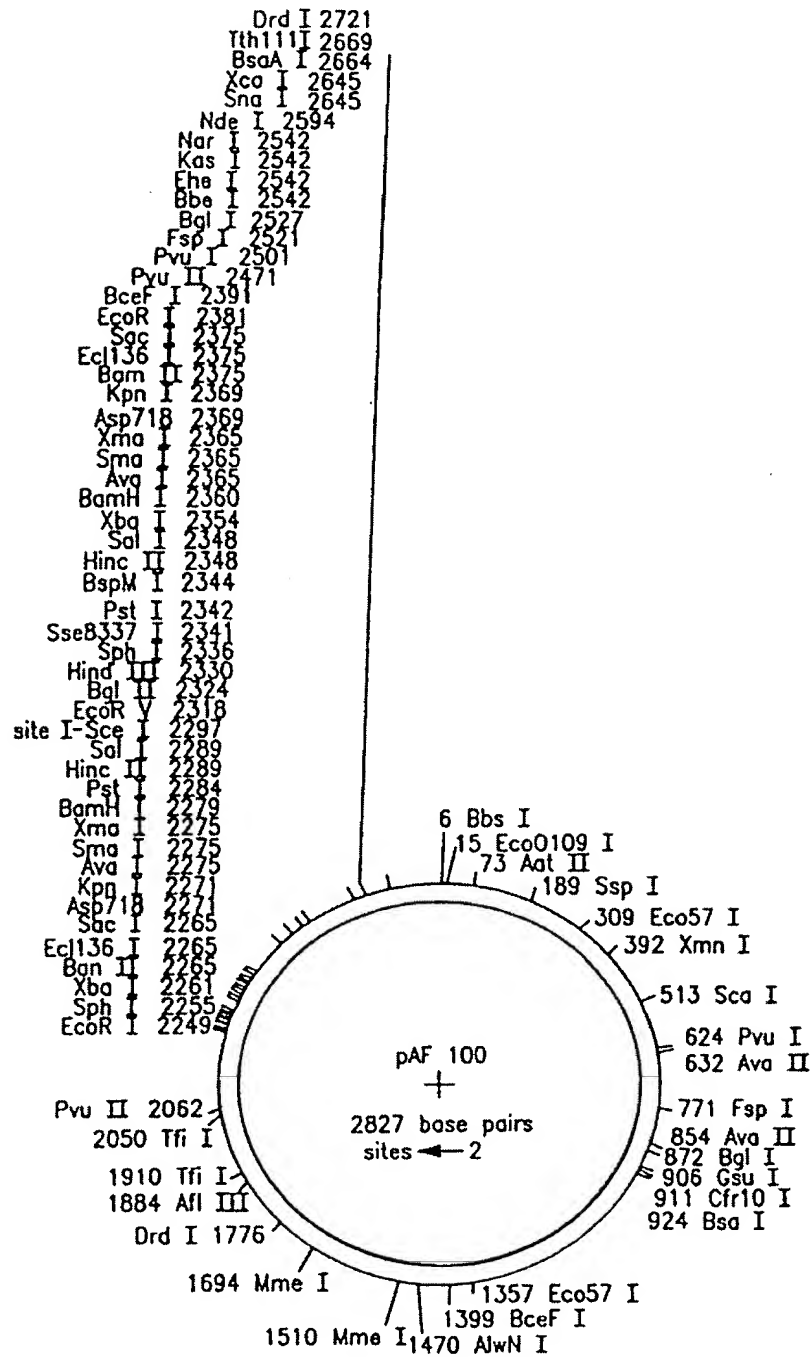
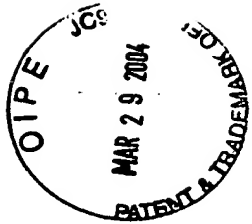


FIG. 9

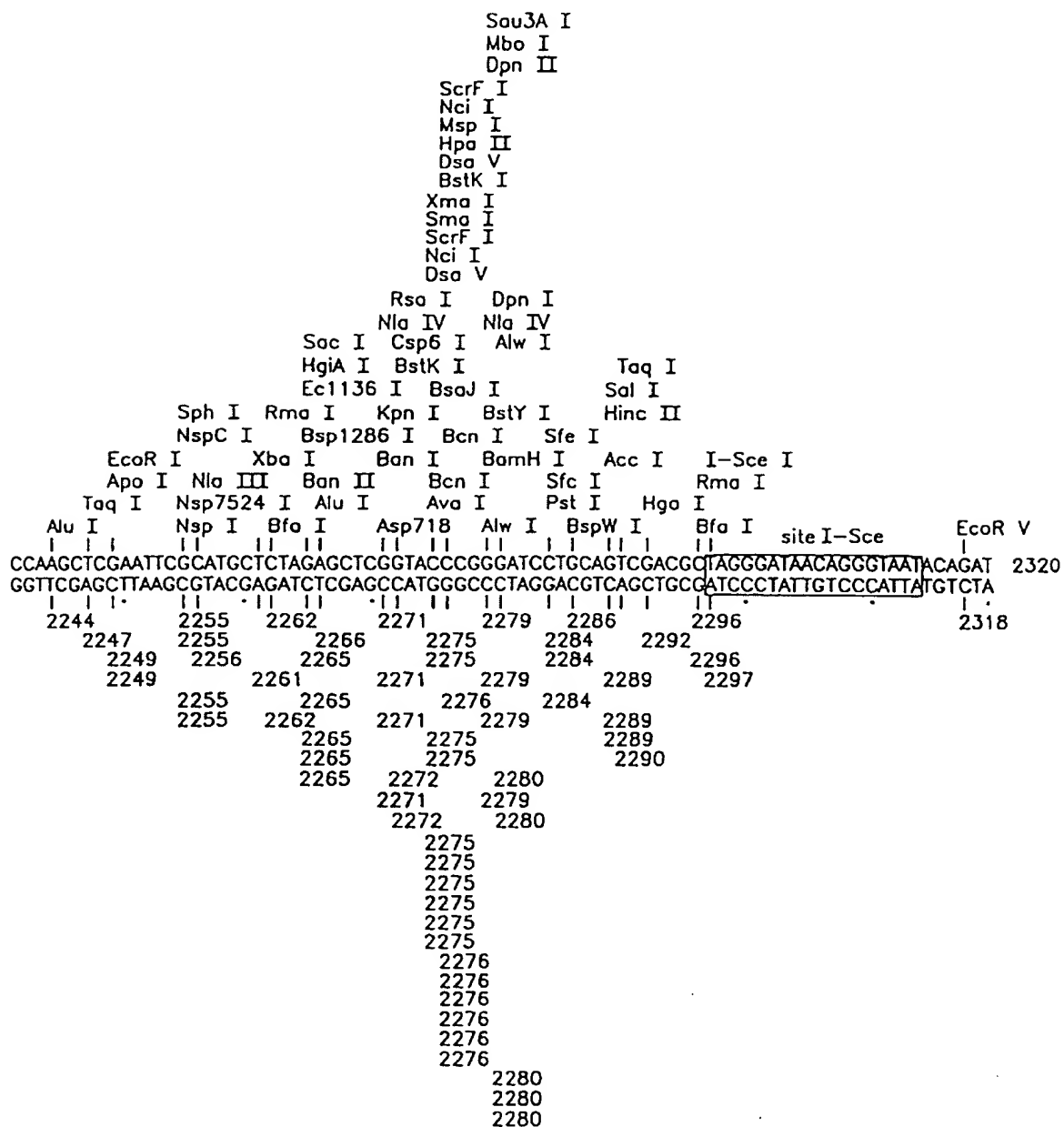
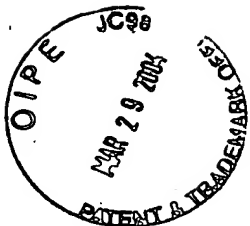


FIG. IOA

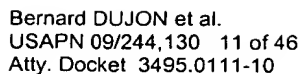
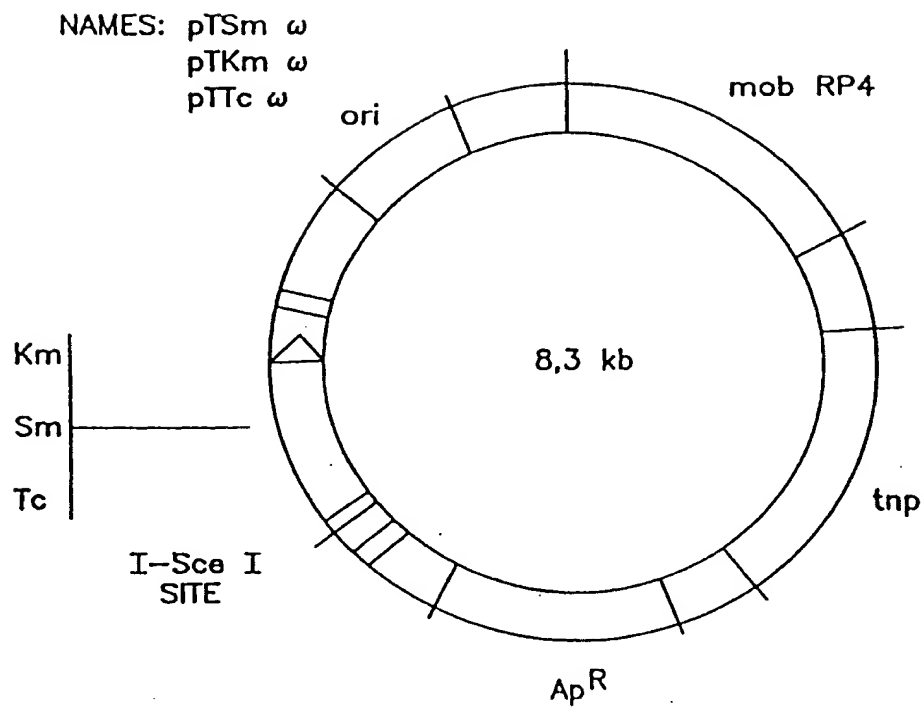
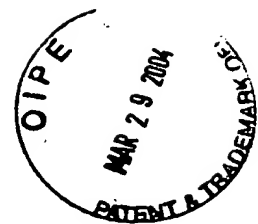


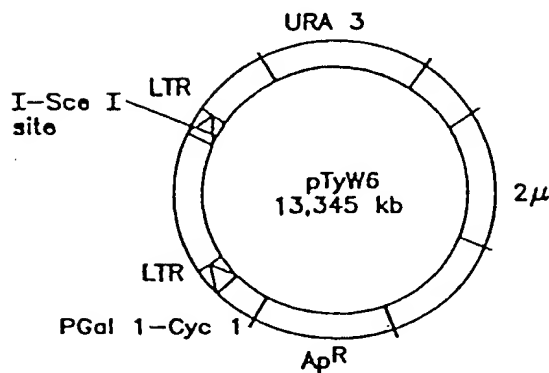
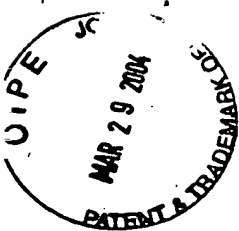
FIG. IOB

FIG. 10B



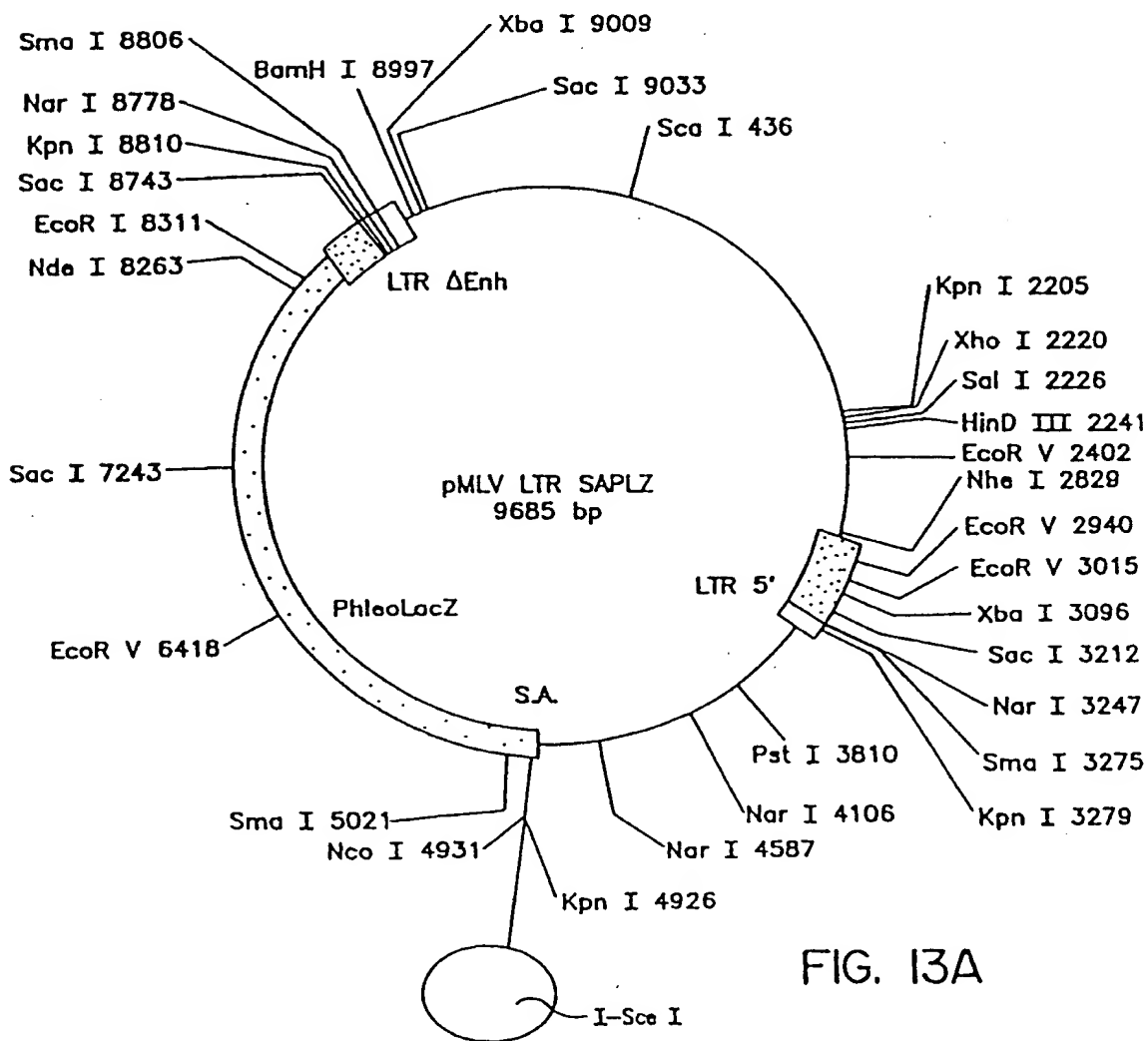
Construction: pGP 704 from De Lorenzo, with transposase gene and insertion of the linker[I-SceI] in NotI unique site

FIG. 11



Construction: pD 123, from J.D. Boeke
with insertion of a linker[I-SceI-NotI] in BamHI

FIG. 12



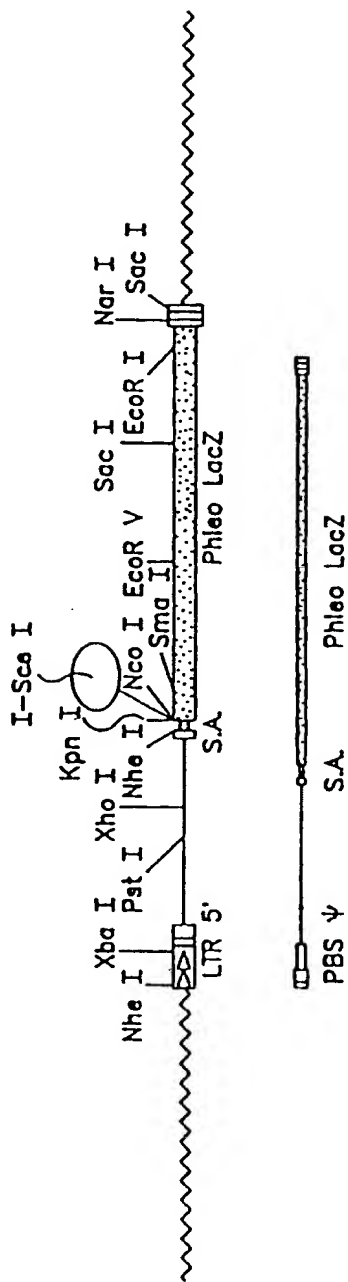


FIG. 13B

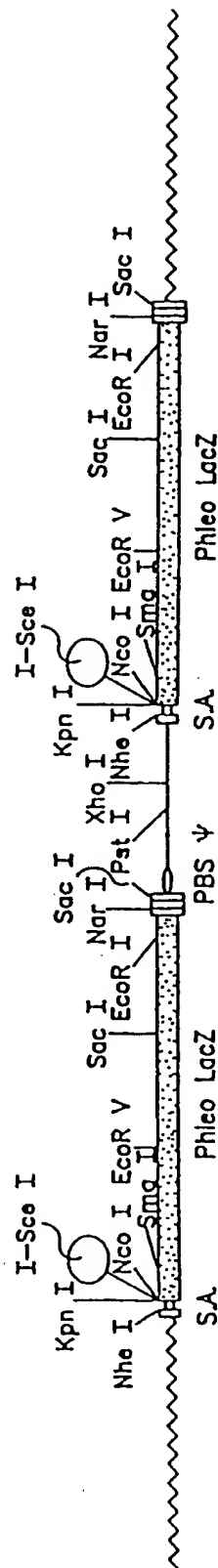


FIG. 13C

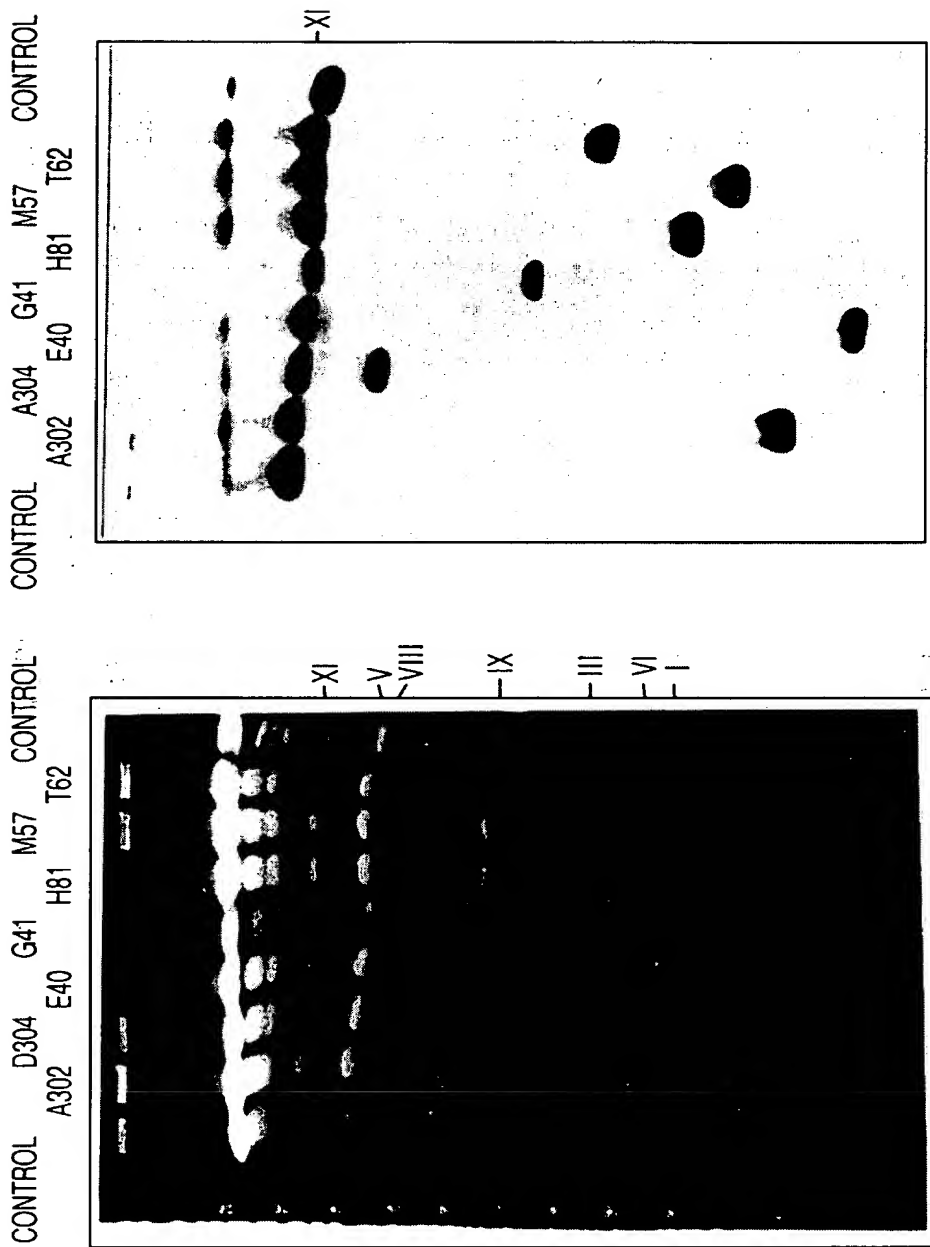


FIG. 14A

FIG. 14B

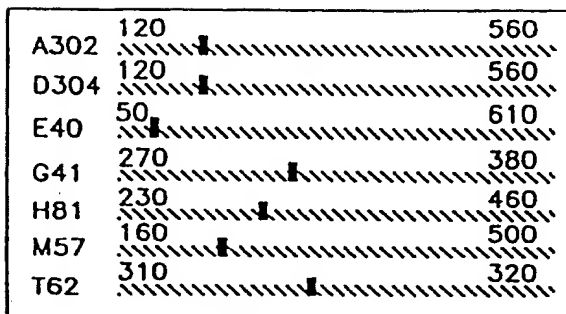


FIG. 15A

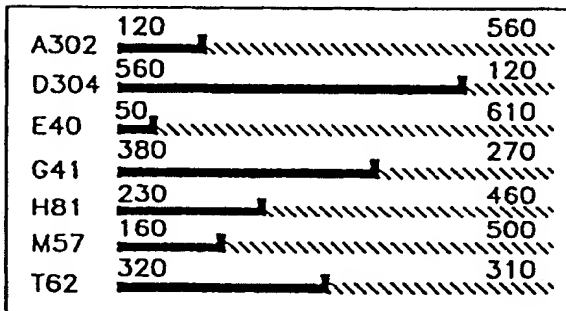


FIG. 15B

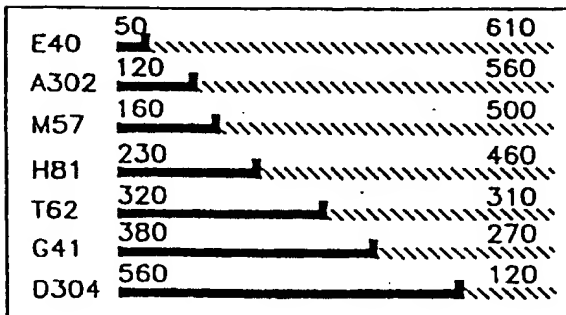


FIG. 15C

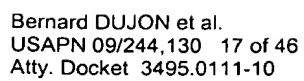


FIG. 15E

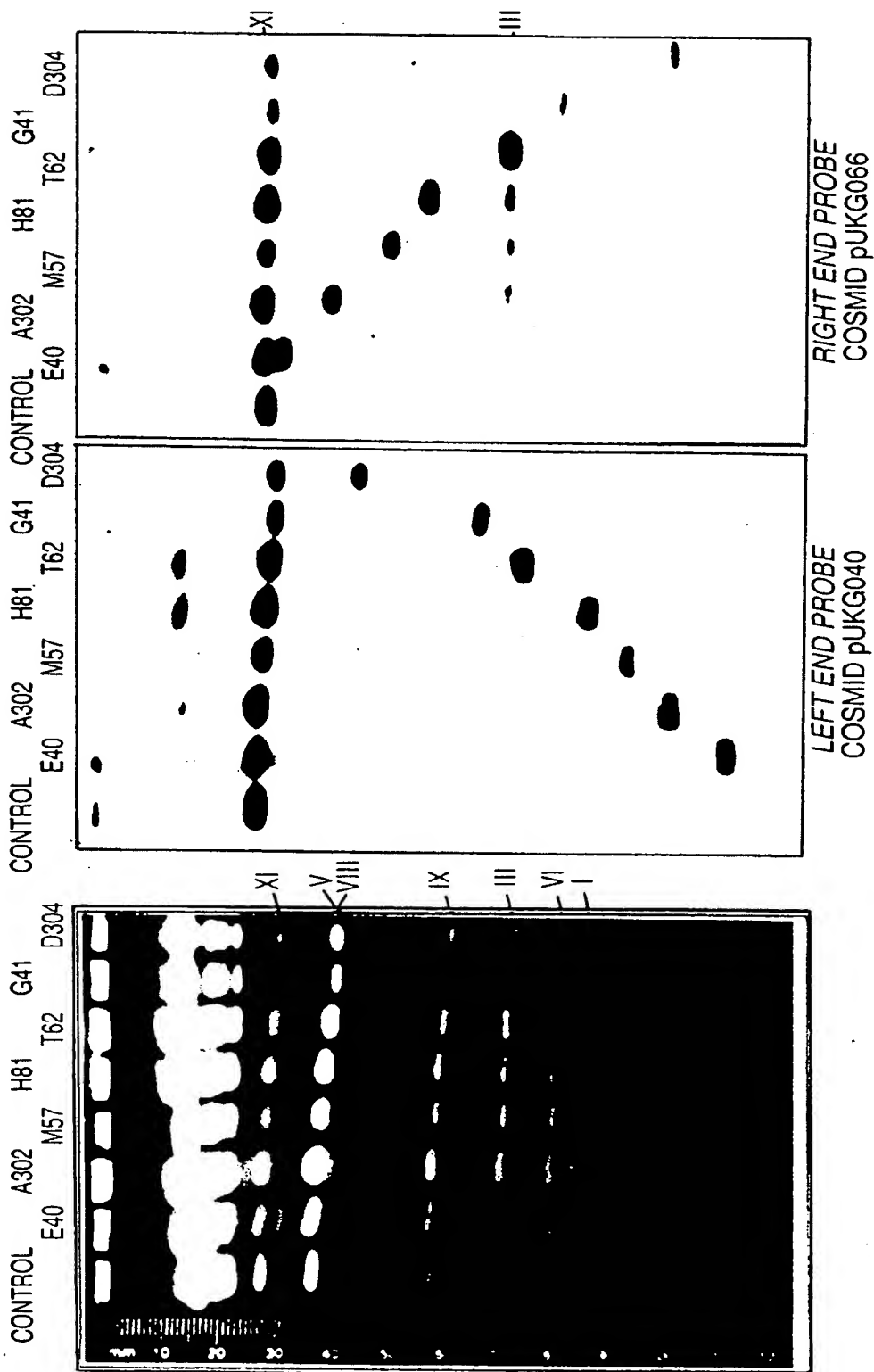
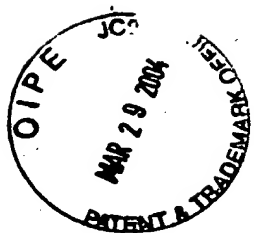
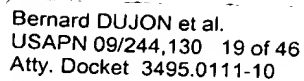


FIG. 16A

FIG. 16B

FIG. 16C



LAD- DER	pEKG 019	pEKG 097	pEKG 081	pEKG 121	pEKG 119	pEKG 021	pEKG 146	pEKG 144	pEKG 046
pEKG 100	pEKG 098	pEKG 090	pEKG 151	pEKG 148	pEKG 011	pEKG 047	pEKG 013	pEKG 118	pEKG 066
	pEKG 019	pEKG 097	pEKG 081	pEKG 121	pEKG 119	pEKG 021	pEKG 146	pEKG 144	pEKG 046

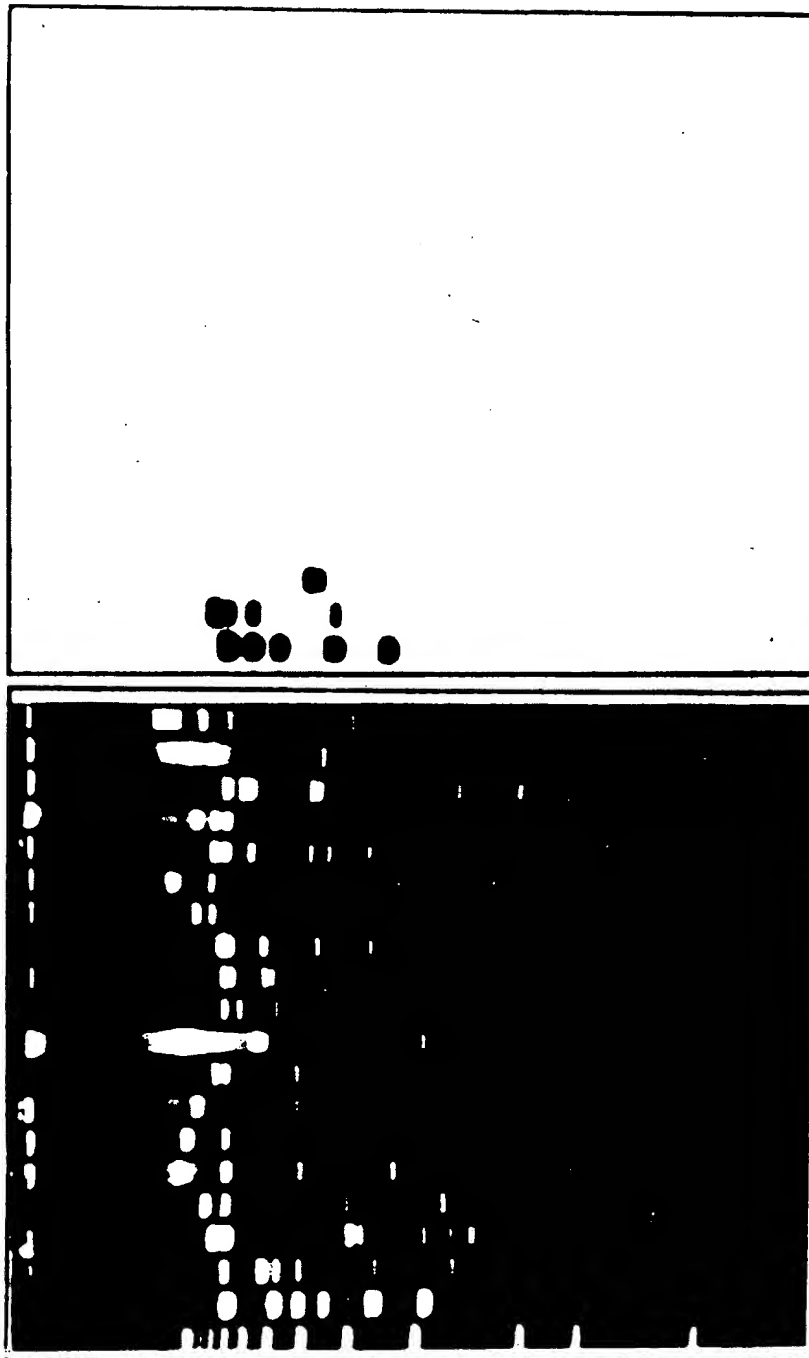
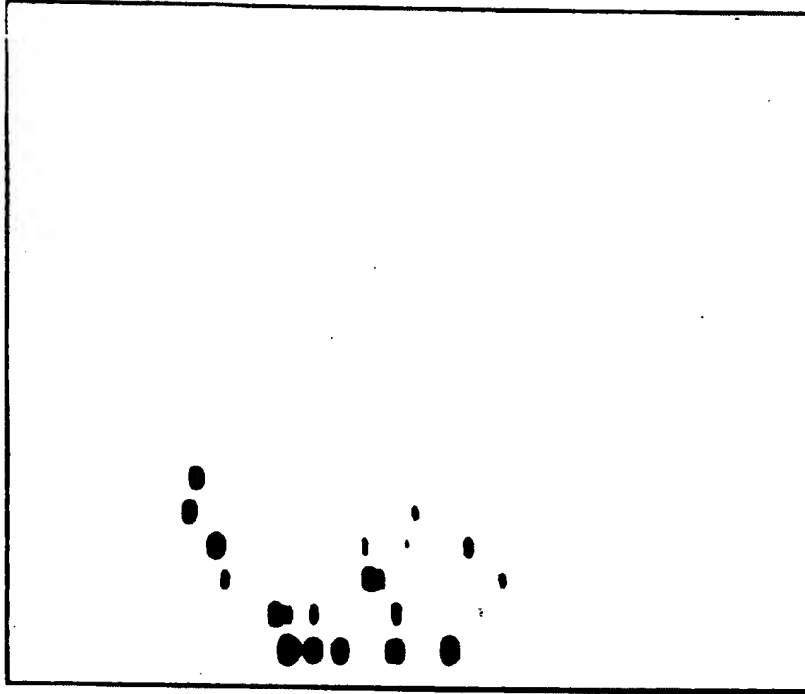
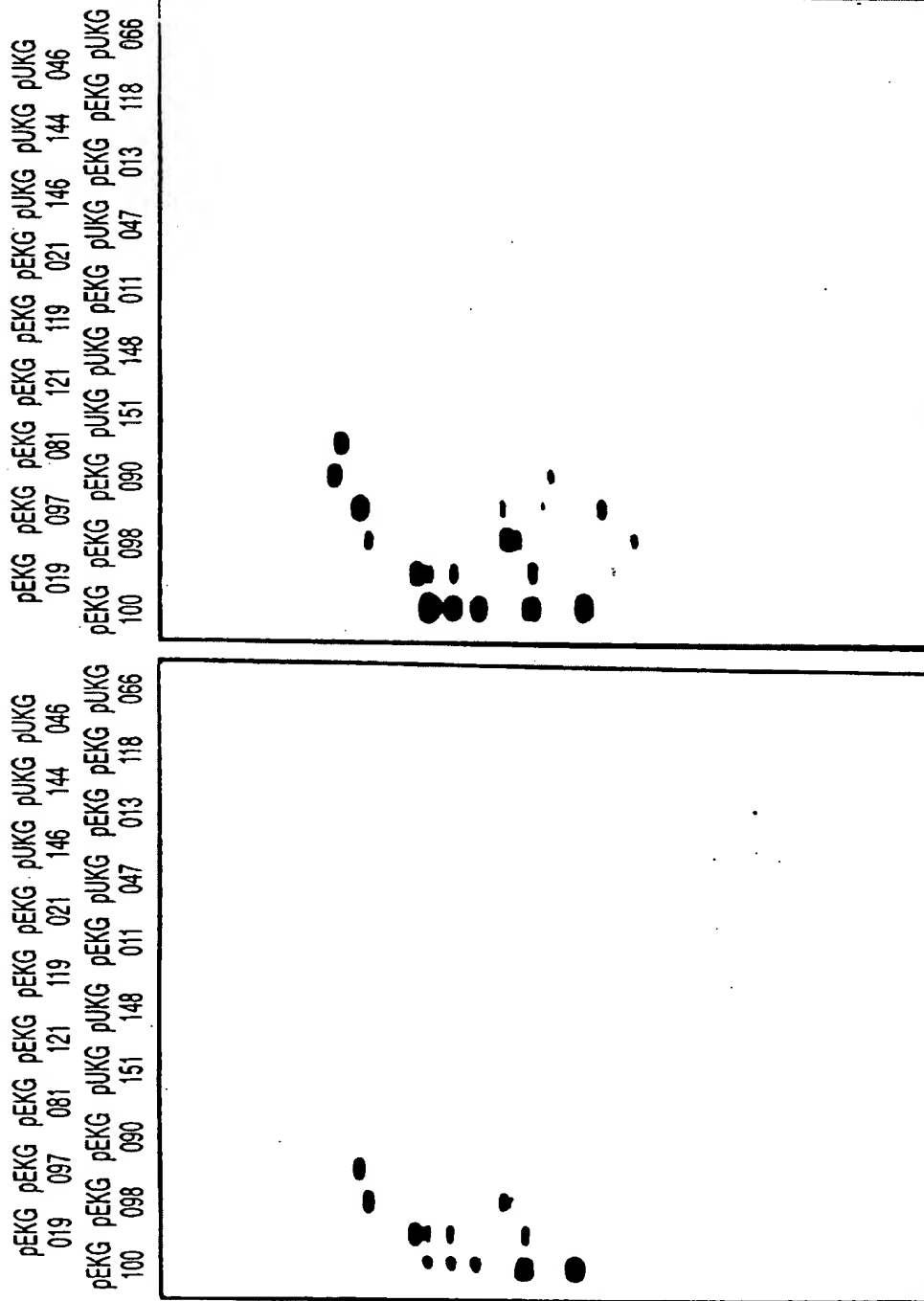
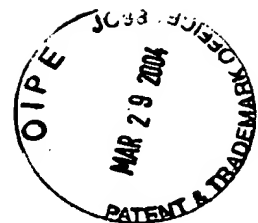


FIG. 17A

FIG. 17B





pKKG pKKG pKKG pKKG pKKG pKKG pKKG pKKG pKKG pKKG	pKKG pKKG pKKG pKKG pKKG pKKG pKKG pKKG pKKG pKKG
019 097 081 121 119 021 146 144 046	019 097 081 121 119 021 146 144 046
pKKG pKKG pKKG pKKG pKKG pKKG pKKG pKKG pKKG pKKG	pKKG pKKG pKKG pKKG pKKG pKKG pKKG pKKG pKKG pKKG
100 098 090 151 148 011 047 013 118 066	100 098 090 151 148 011 047 013 118 066

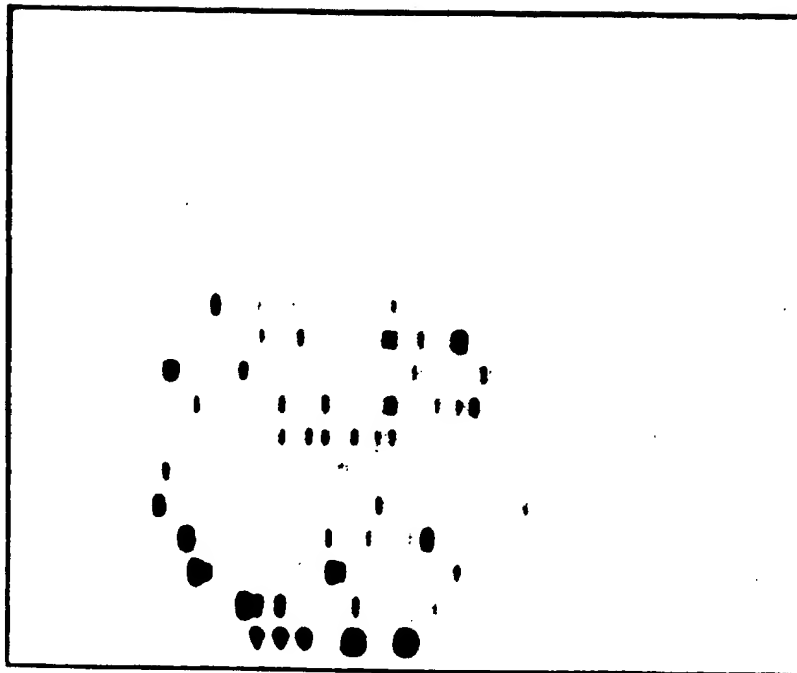


FIG. 17F

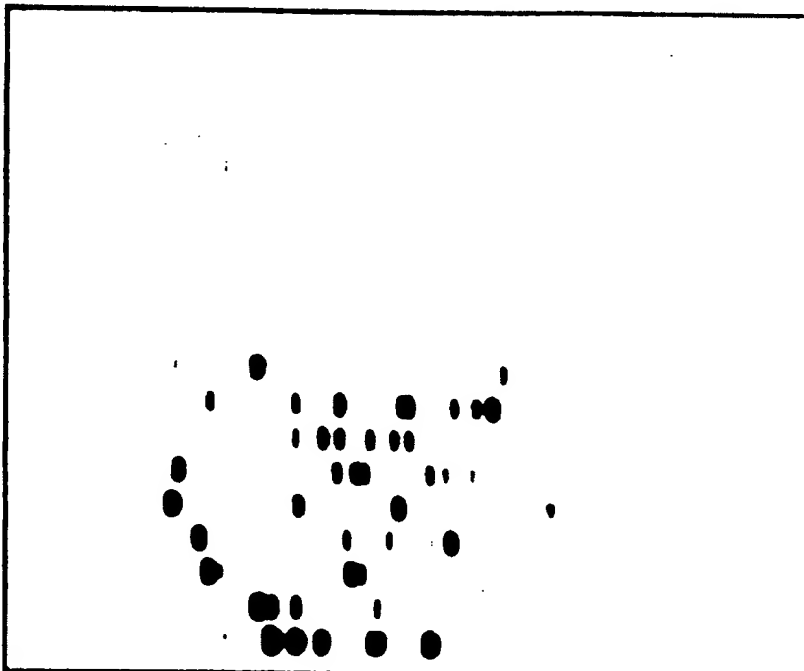


FIG. 17E

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PEKG PEKG PEKG PEKG PEKG PEKG PEKG PEKG PEKG PEKG PEKG PEKG PEKG PEKG PEKG
019 097 081 121 119 021 146 144 046
PEKG PEKG PEKG PEKG PEKG PEKG PEKG PEKG PEKG PEKG PEKG PEKG PEKG PEKG PEKG
100 098 090 151 148 011 047 013 118 066

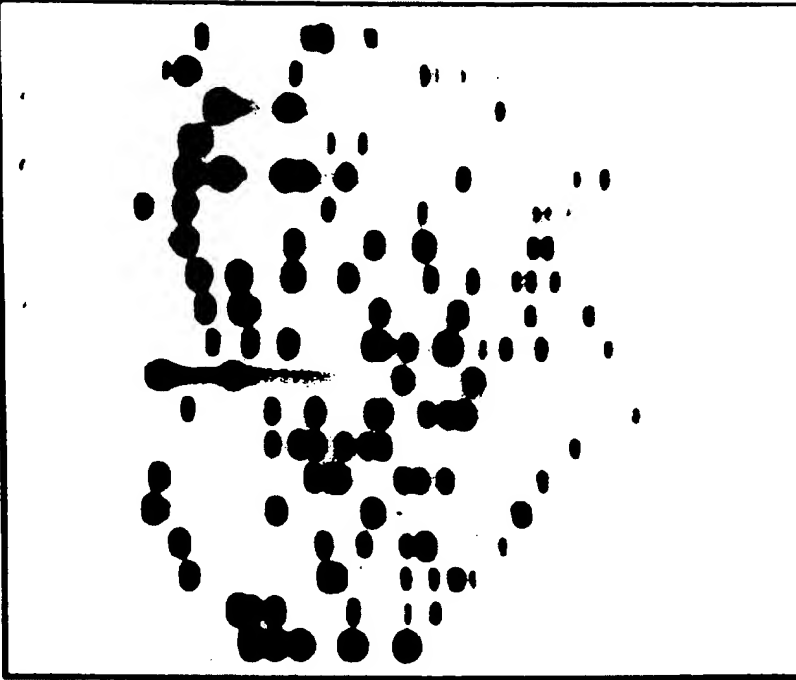


FIG. 17G

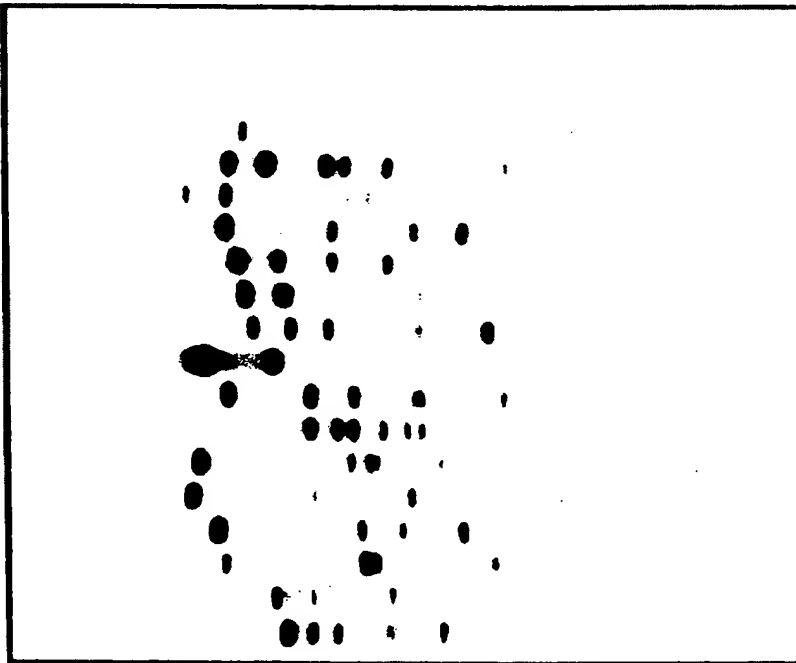


FIG. 17H

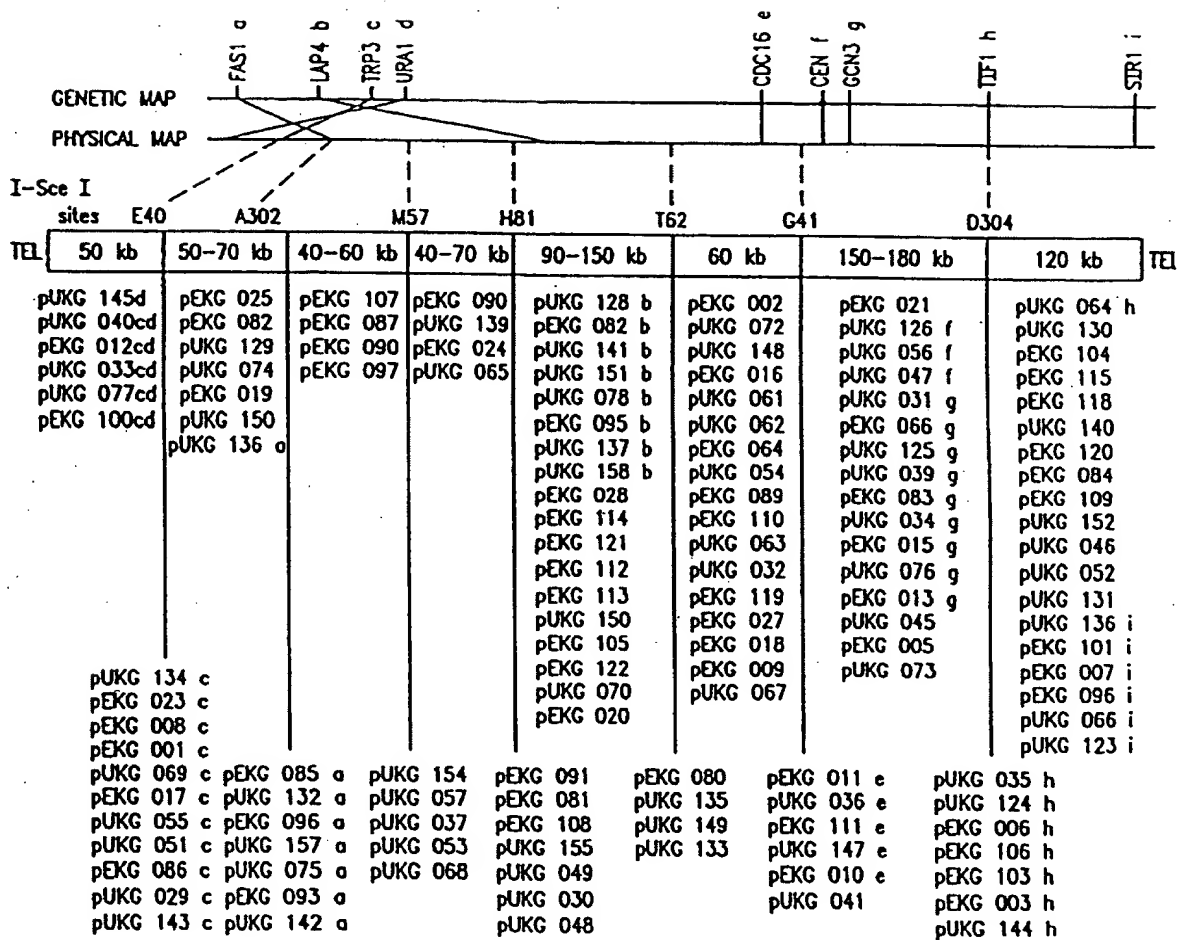
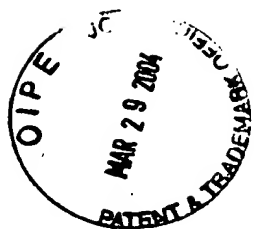


FIG. 18

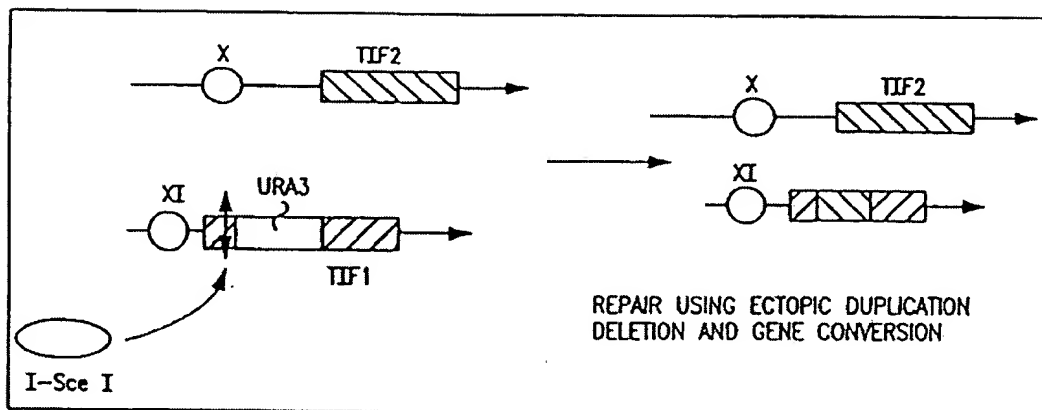
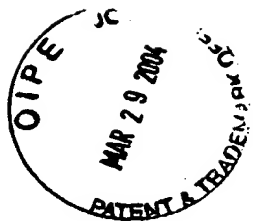


FIG. 19A

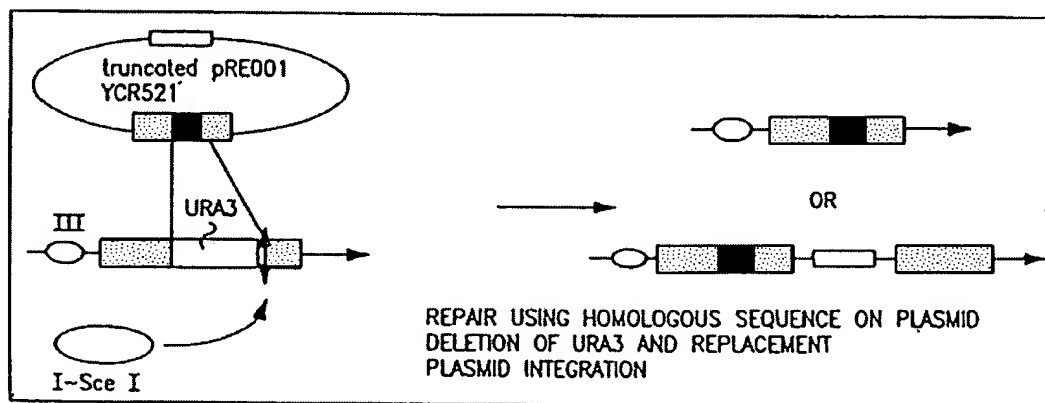
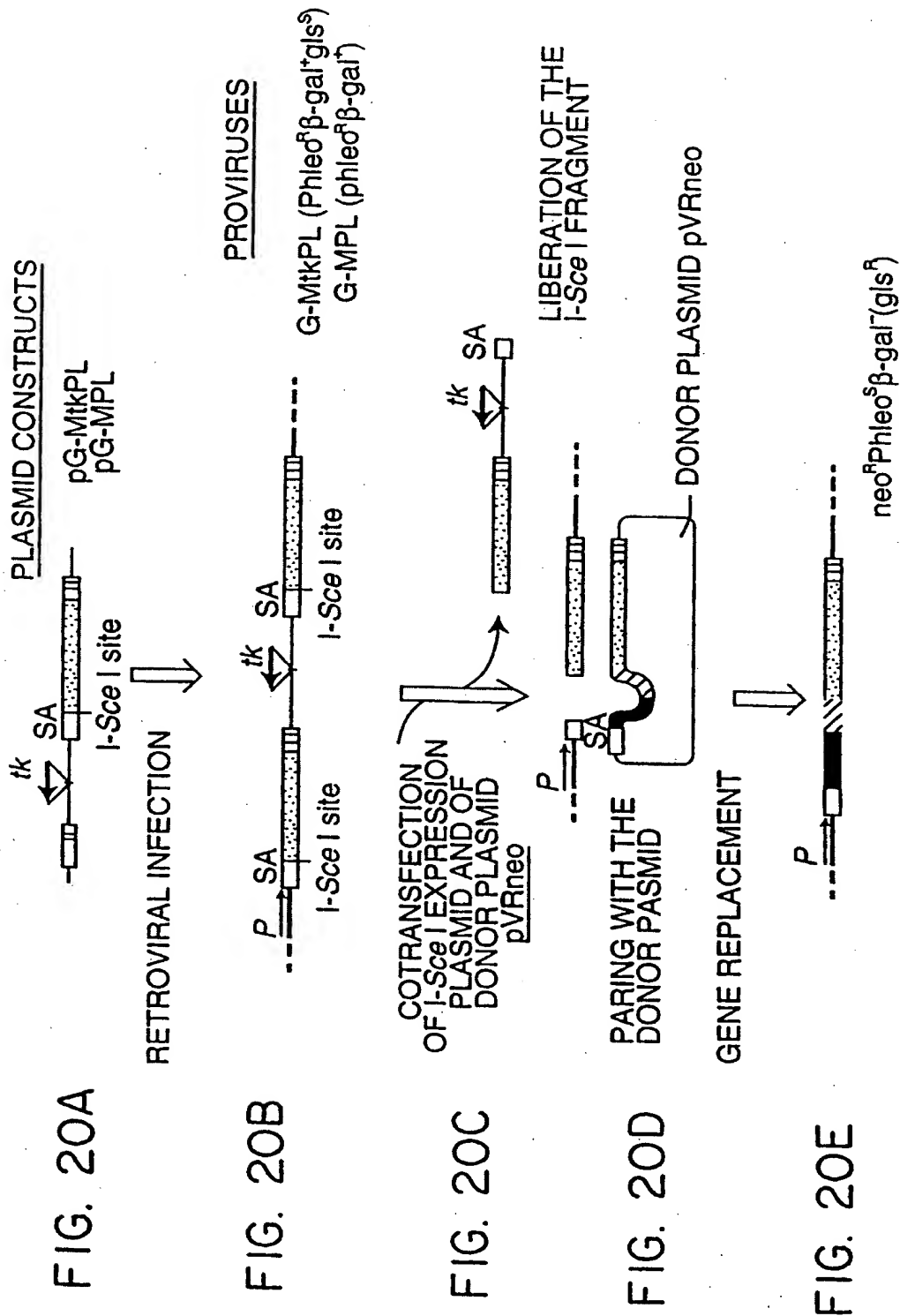
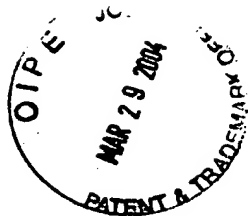


FIG. 19B



LTR
 PhleoLacZ
 NEO
 POLY A
 GENOMIC DNA
 tk THYMIDINE KINASE

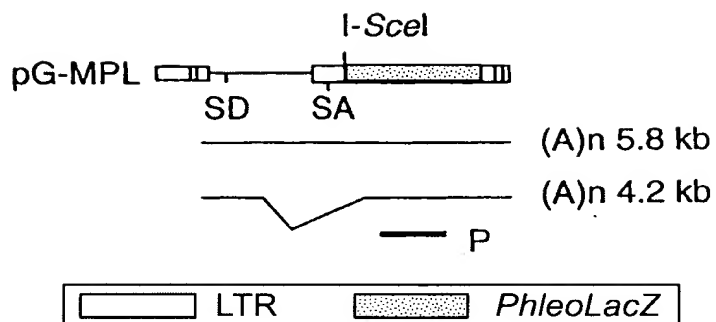
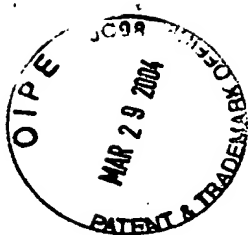


FIG. 2IA

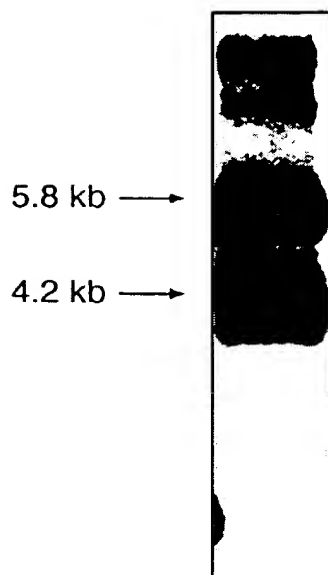
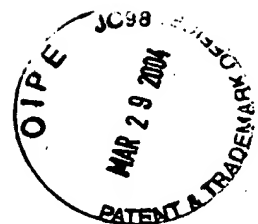
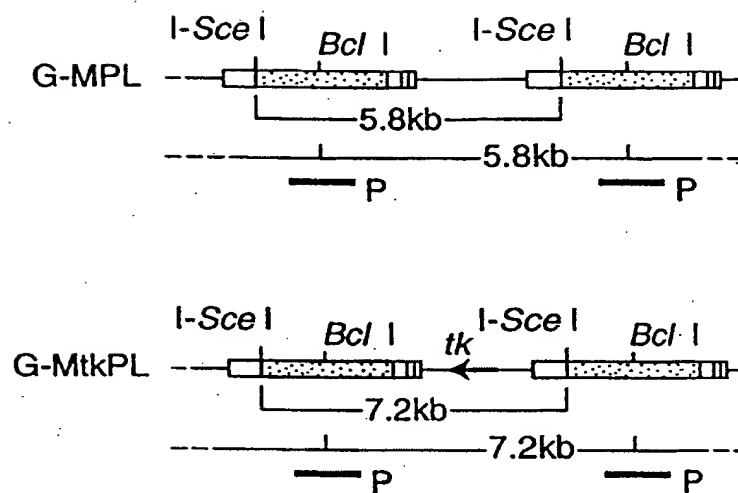
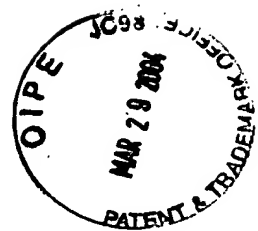


FIG. 21B



LTR
 PhleoLacZ

←
 tk THYMIDINE KINASE

FIG. 22A

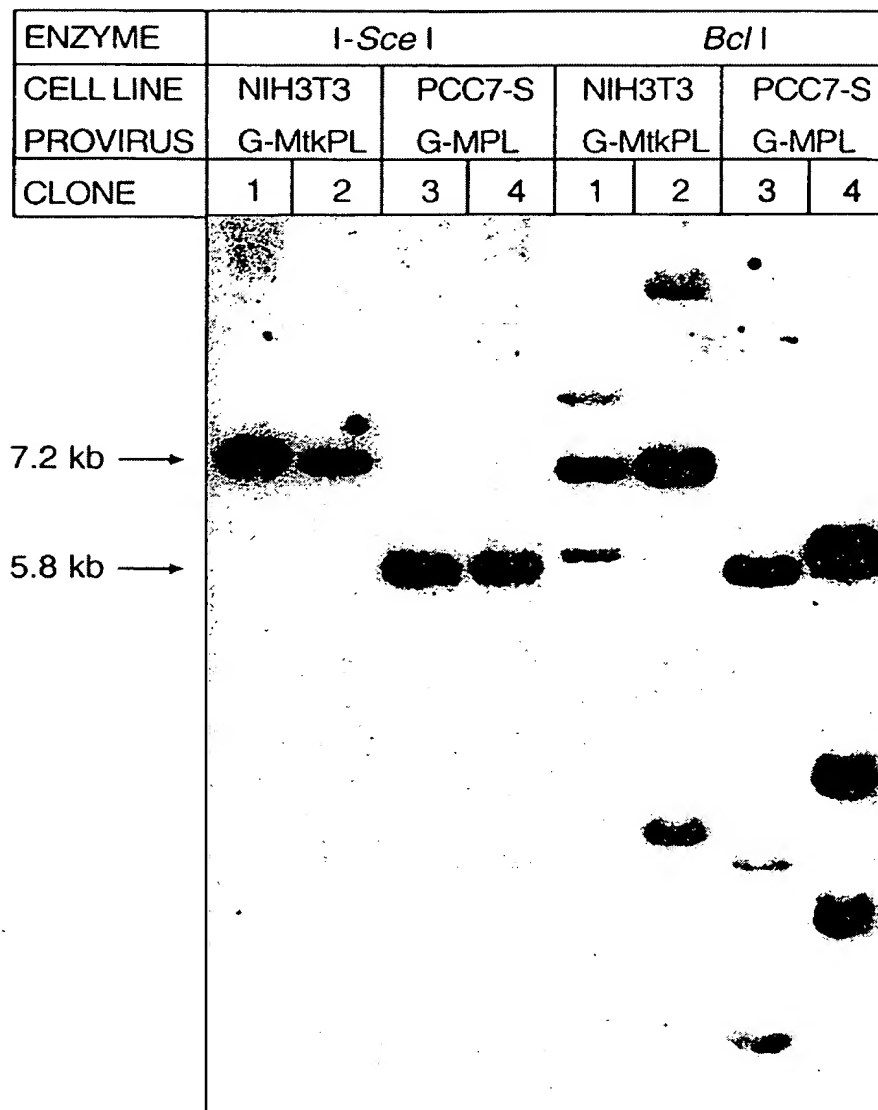
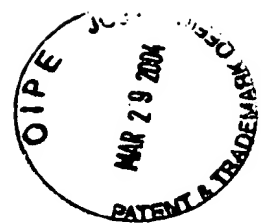


FIG. 22B

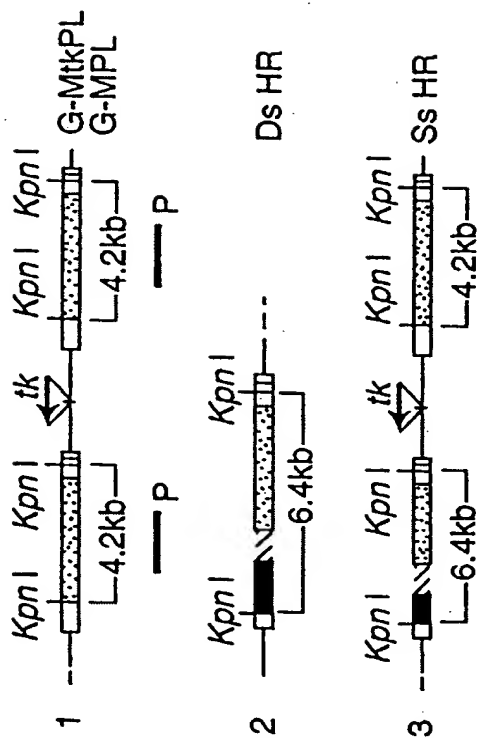
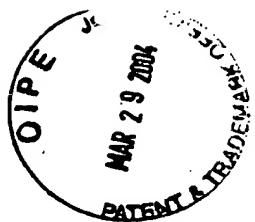


FIG. 23A

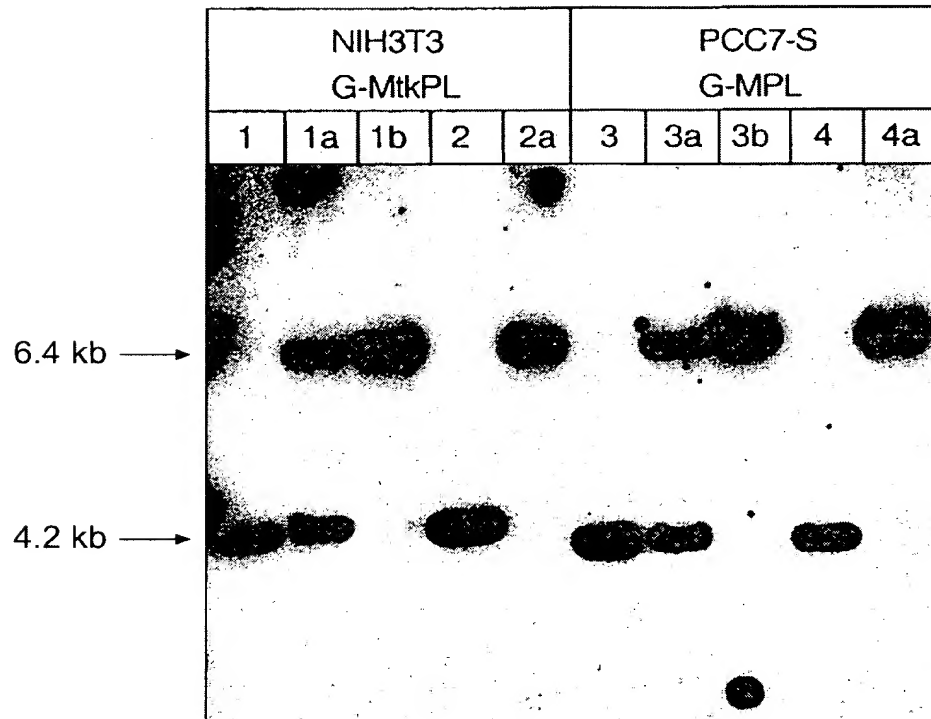
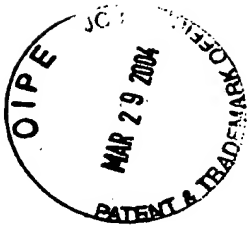
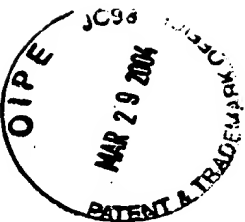


FIG. 23B



PCC7-S / G-MPL, CLONE 3

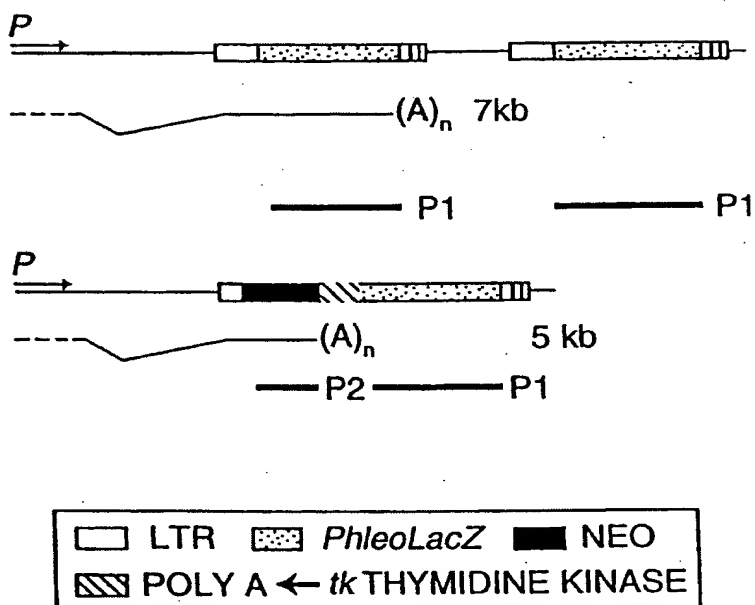


FIG. 24A

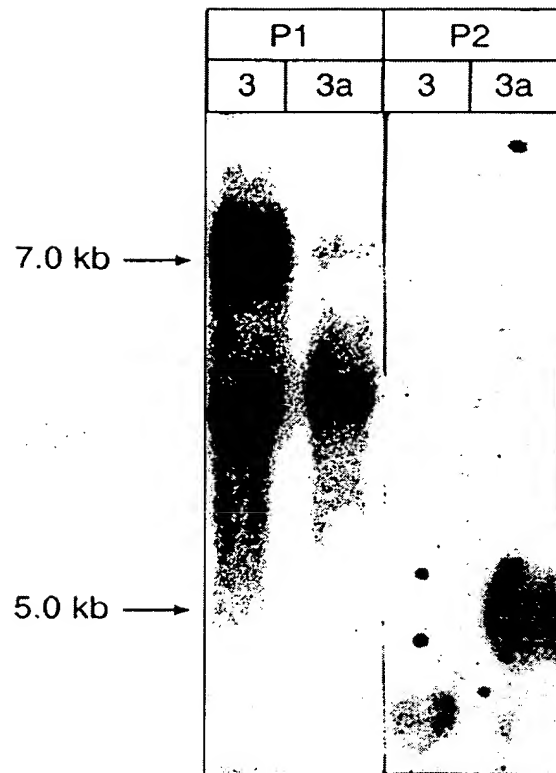
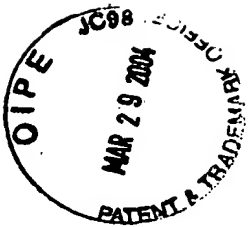


FIG. 24B



A. CHROMOSOMAL DNA
CONTAINING PROVIRUS

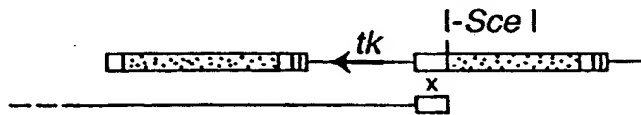
PHENOTYPES



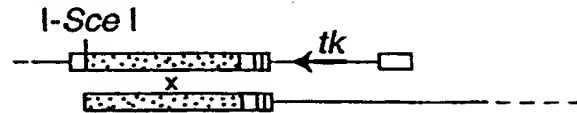
TRANSFECTION BY
I-Sce I ENDONUCLEASE
EXPRESSION VECTOR

B. INTRA-CHROMOSOMAL
RECOMBINATIONS EVENTS

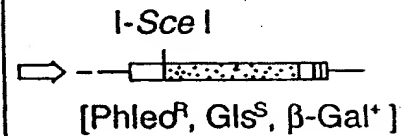
1. THE LEFT I-Sce I IS CUT.
PAIRING AND RECOMBINATION



2. THE RIGHT I-Sce I IS CUT.
PAIRING AND RECOMBINATION



3. BOTH I-Sce I SITES ARE CUT.
RELIGATION BY END-JOINING



C. INTER-CHROMOSOMAL RECOMBINATION EVENT

BOTH I-Sce I SITES ARE CUT. GAP REPAIR USING INTACT
CHROMOSOME SEQUENCES

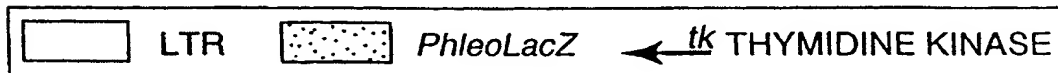
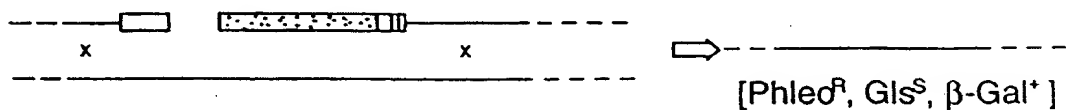
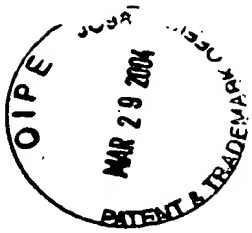


FIG. 25



A. PARENTAL DNA, G-MtkPL

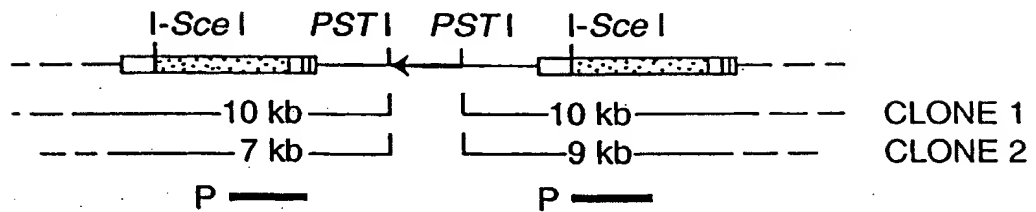


FIG. 26A

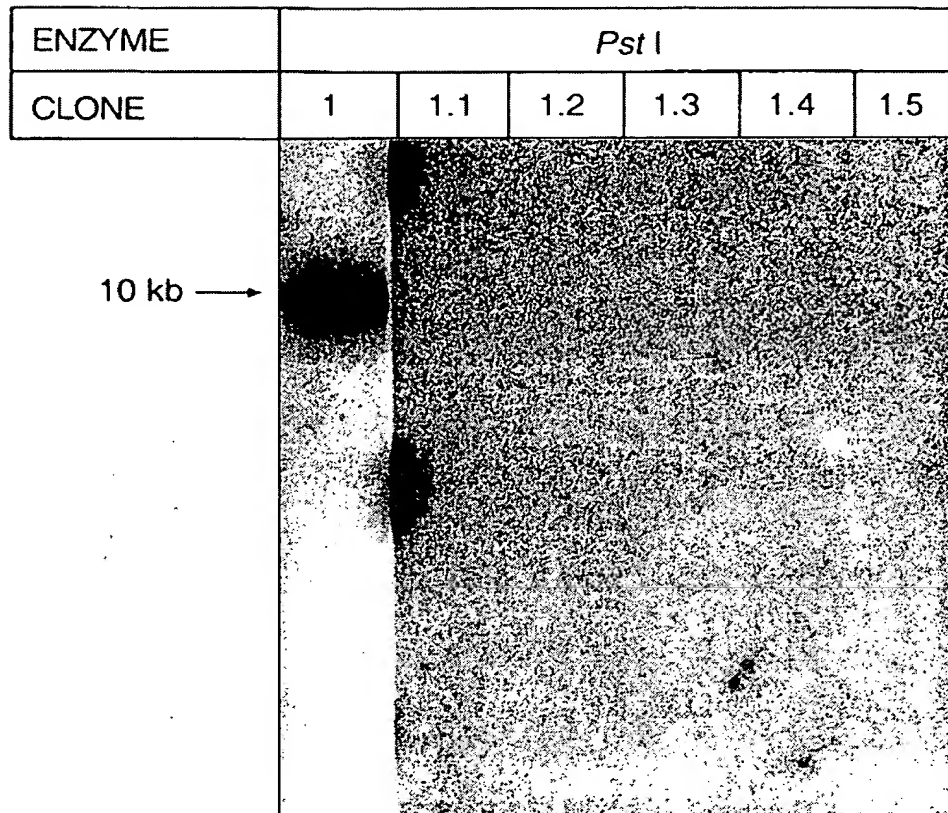
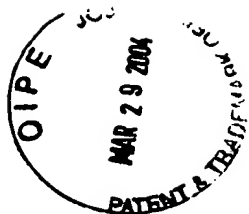


FIG. 26B

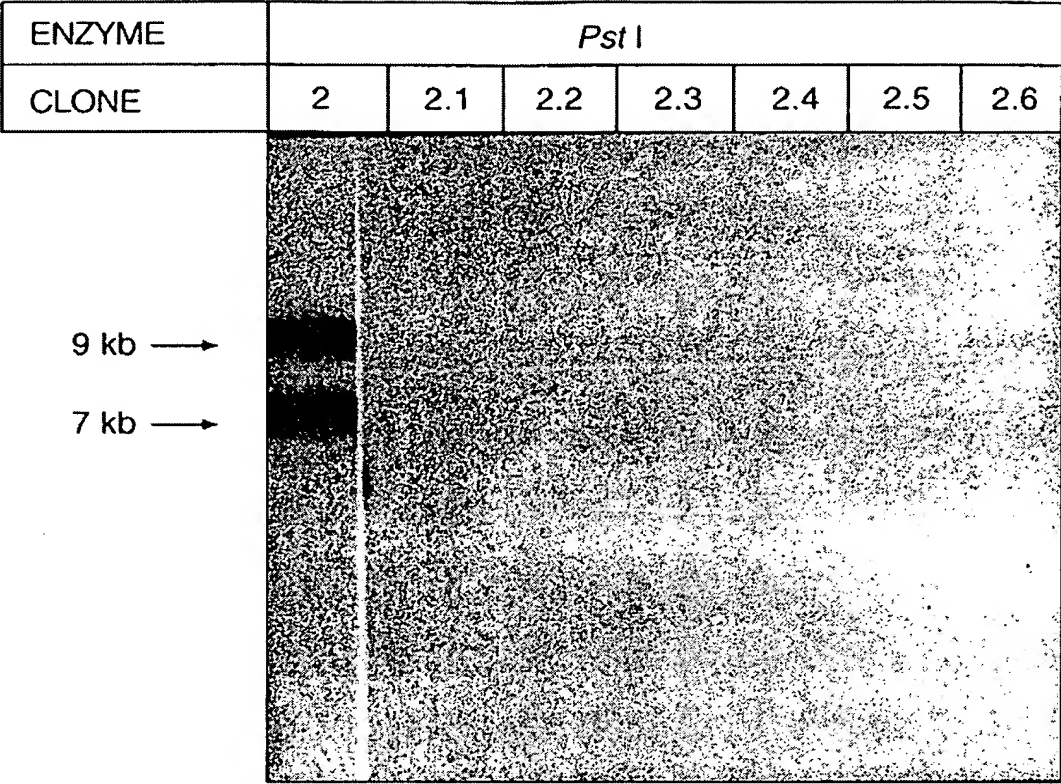
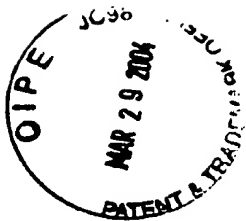
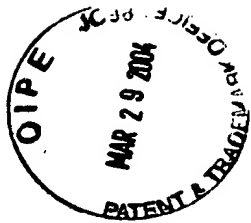
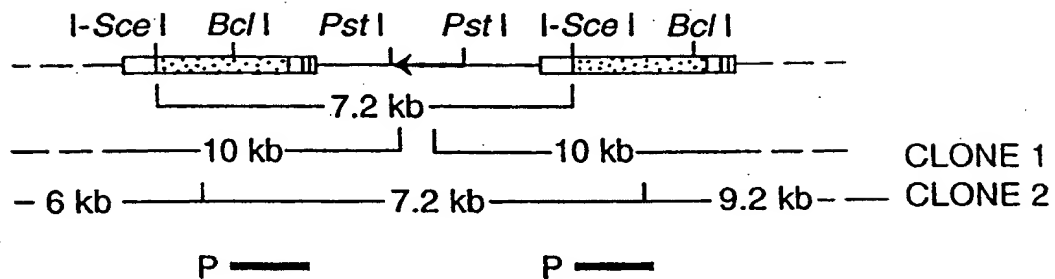


FIG. 26C



1. PARENTAL DNA, G-MtkPL



2. INTRA-MOLECULAR RECOMBINATION EVENT

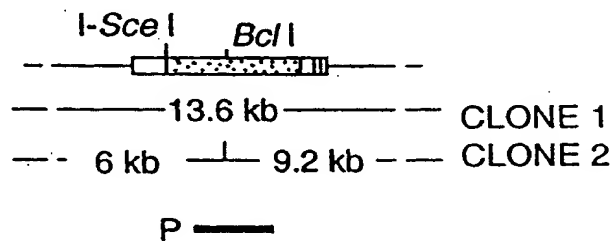


FIG. 27A

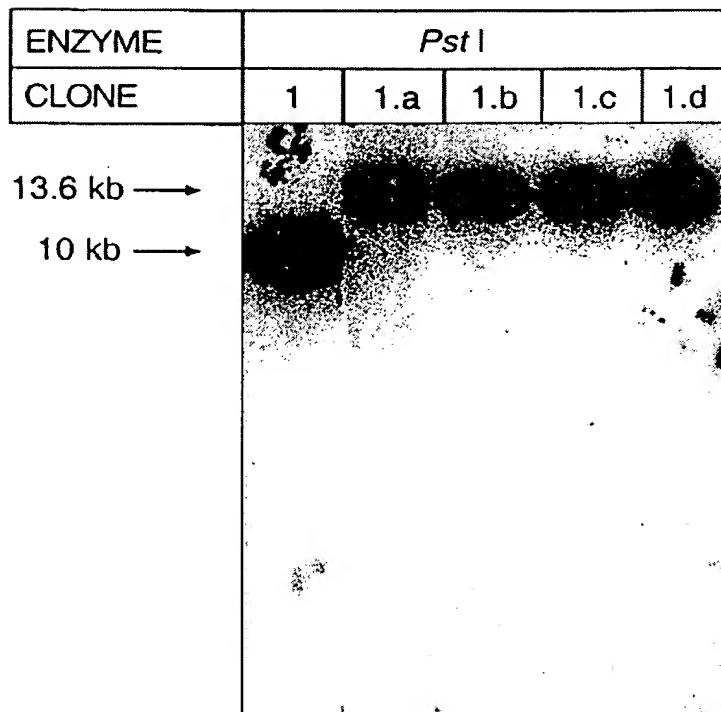
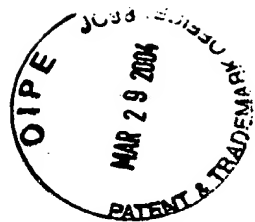


FIG. 27B

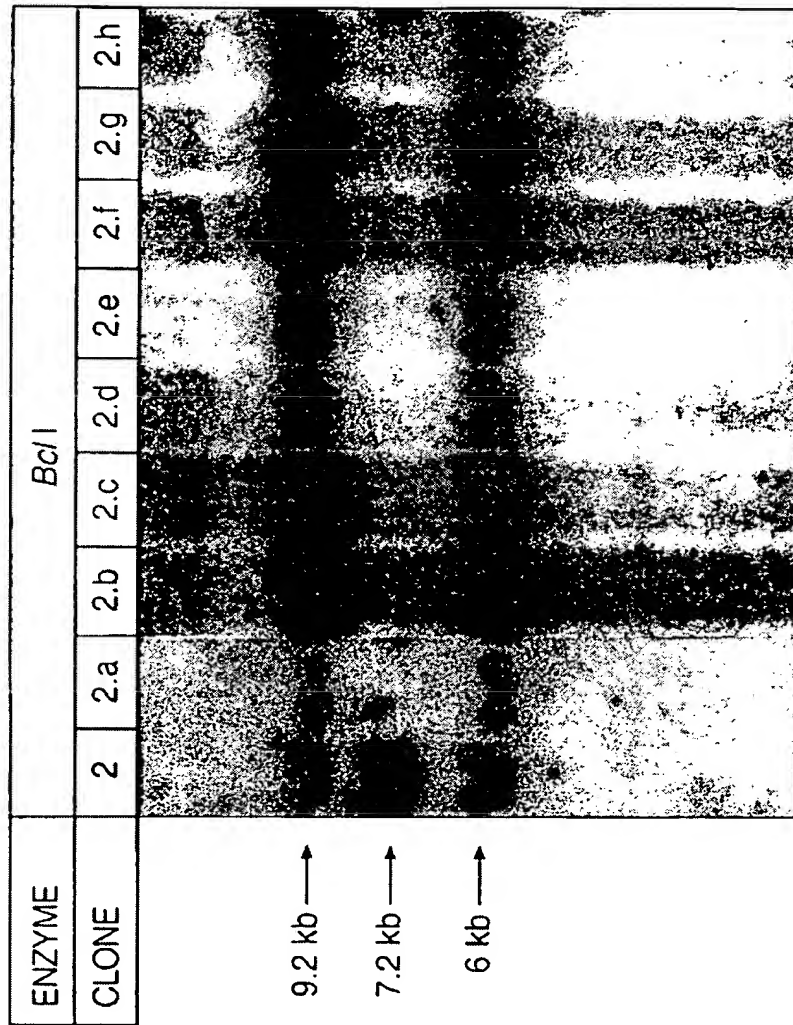
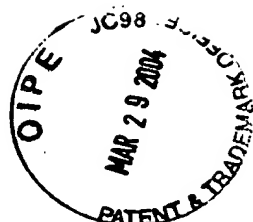
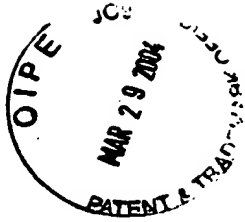
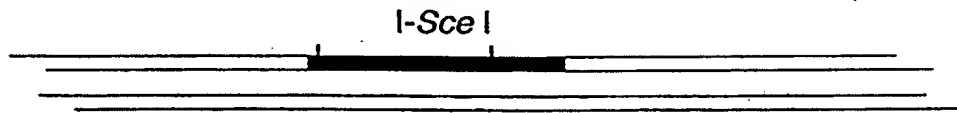


FIG. 27C



LOSS OF HETEROZYGOSITY

INTEGRATION OF ARTIFICIAL SITE OR
PRESENCE OF SPECIFIC SITE



EXPRESSION OF I-Sce I AND SPECIFIC CLEAVAGE



REPAIR OF THE DSB WITH THE OTHER CHROMATID

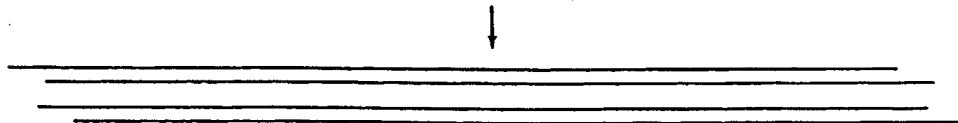
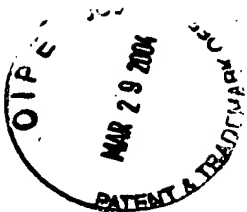


FIG. 28



CONDITIONAL ACTIVATION (TANDEM REPEAT)

INTEGRATION OF ARTIFICIAL SITE BETWEEN TANDEM REPEATS



GENE X INACTIVE

EXPRESSION OF I-Sce I AND SPECIFIC CLEAVAGE

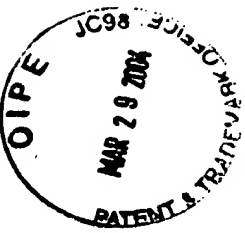


REPAIR OF THE DSB BY SINGLE STRAND ANNEALING



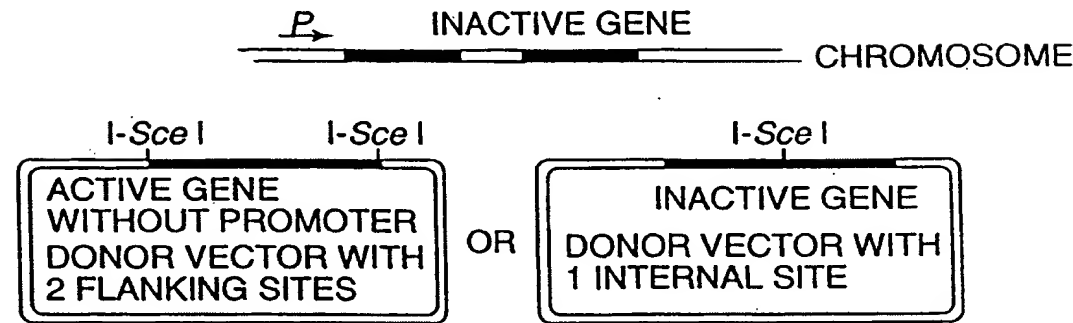
GENE X ACTIVE

FIG. 29

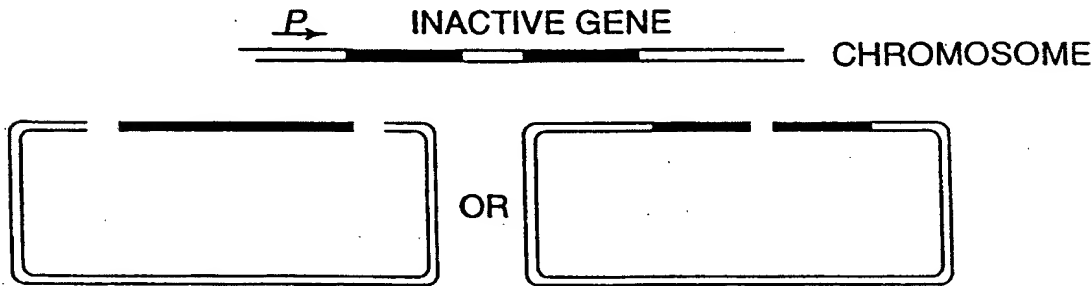


ONE STEP REARRANGEMENT

INTEGRATION OF ARTIFICIAL SITE OR
PRESENCE OF SPECIFIC SITE



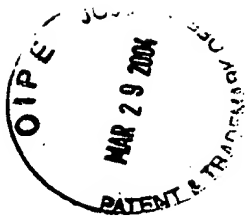
EXPRESSION OF I-Sce I ENZYME
AND
SPECIFIC CLEAVAGE OF THE DONOR PLASMID



RECOMBINATION BETWEEN THE CHROMOSOME AND PLASMID

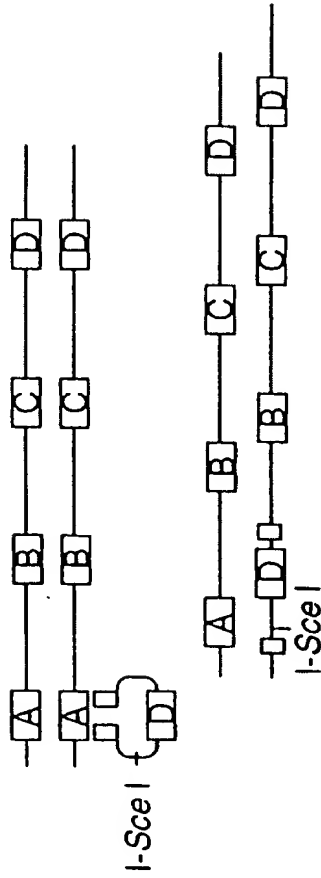


FIG. 30



DUPLICATION OF A LOCUS

1. INSERTION OF I-Sce I SITE BY CLASSICAL GENE REPLACEMENT



2. SPECIFIC CLEAVAGE BY I-Sce I ENZYME AND REPAIR OF THE BREAK BY HOMOLOGOUS SEQUENCES

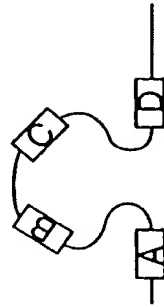
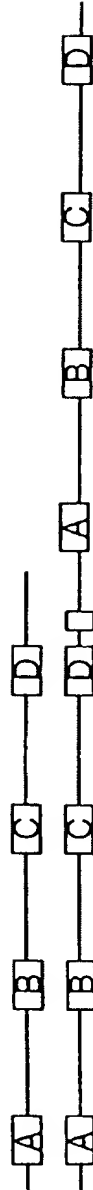


FIG. 3I

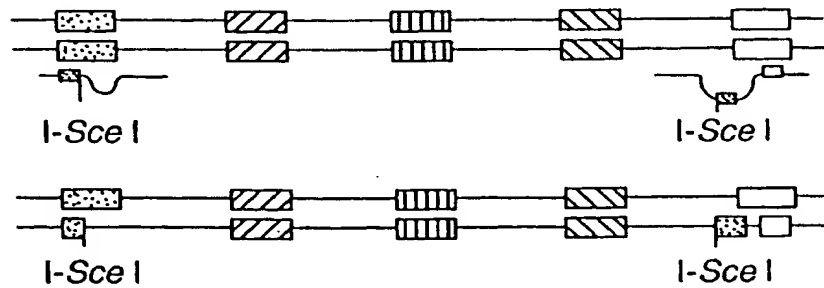
3. DUPLICATION OF THE TOTALITY OF THE LOCUS



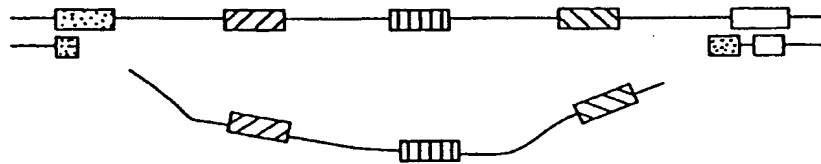


DELETION OF A LOCUS

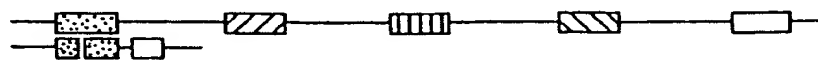
1 INSERTION OF TWO I-Sce I SITES FLANKING THE LOCUS



2 EXPRESSION OF THE ENZYME AND CLEAVAGE



3 RECOMBINATION BETWEEN THE TWO ENDS



4 DELETION OF THE LOCUS

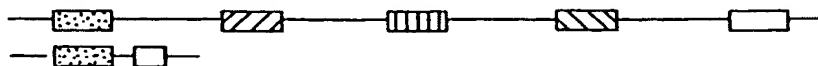


FIG. 32

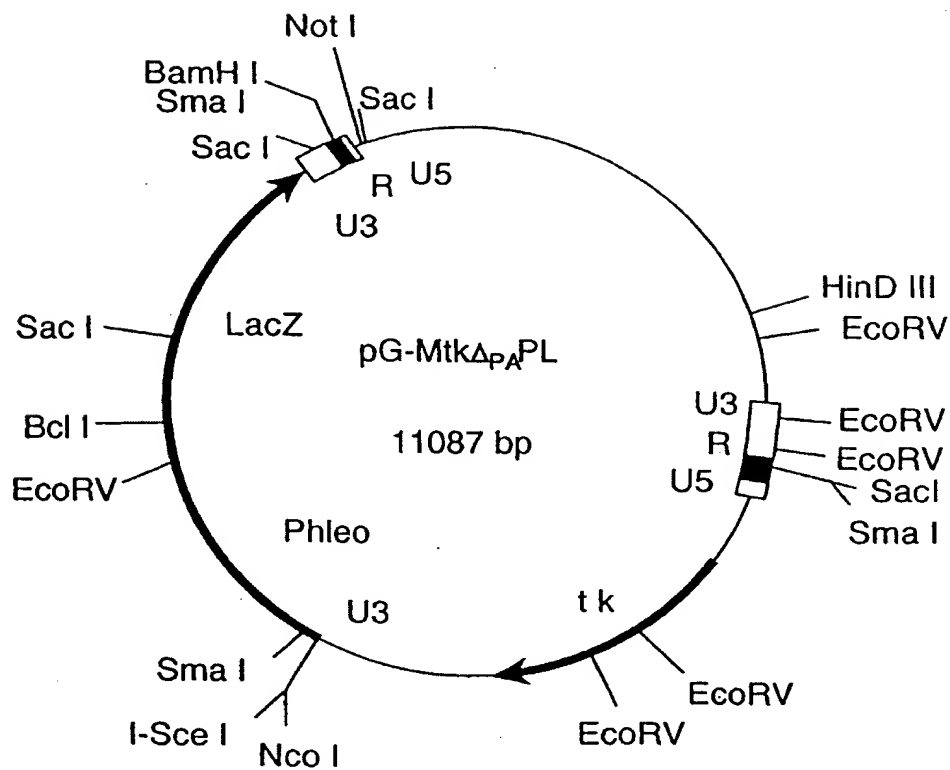
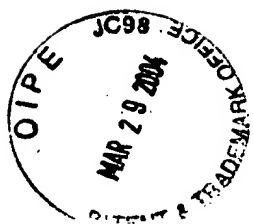


FIG. 33